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US High Production Volume Chemical Program

Category Summary

For

Crude Butadiene C4 Category

Prepared by:

Olefins Panel of the American Chemistry Council

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EXECUTIVE SUMMARY

The Olefins Panel of the American Chemistry Council (ACC) hereby submits the category summary report for the Crude Butadiene C4 Category under the Environmental Protection Agency's High Production Volume (HPV) Chemical Challenge Program (Program). The purpose of this report is to:

- Present results of an assessment to determine whether four production streams can be adequately characterized with existing data and additional data as described in the Crude Butadiene C4 Category test plan.
- Summarize the SIDS (Screening Information Data Set) physicochemical, environmental fate and effects, and human health HPV Program endpoints for the Crude Butadiene C4 Category.
- Provide a description of manufacturing processes, potential exposure sources, and uses for Crude Butadiene C4 streams.

The Crude Butadiene C4 Category originally contained four streams. After all data were evaluated to determine whether the streams formed a cohesive category, it was decided that two streams, Pyrolysis C3+ and Pyrolysis C4+, should be considered a separate category based on composition and effects of stream constituents, which are not shared by all four streams. Therefore, these two streams were removed from this category. A category summary report characterizing their HPV Program endpoints will be prepared and submitted separately. Consequently, the following category report summarizes HPV Program data for the C4 Crude Butadiene and Butadiene Unit Heavy Ends streams, which constitute the revised Crude Butadiene C4 Category.

The two streams retained in the Crude Butadiene C4 Category consist of a complex mixture of hydrocarbons. The typical carbon (C) number distribution for these streams ranges predominantly between C3 and C5. Much of the data used to characterize this category are from 1,3-butadiene, which is the most chemically reactive of the constituents and hence presumed the most biologically active component and major contributor to toxicological activity. This chemical is present in the two streams covered by this category at concentrations between approximately 10 to 92% (by weight).

Exposure

Industrial emissions of chemicals such as 1,3-butadiene are reported annually to the EPA and made available to the public in the Toxics Release Inventory (TRI). The TRI data indicate that industrial emissions of 1,3-butadiene have declined by 69% since 1988 or from 7.7 million pounds to 2.4 million pounds per year in 2000.

Fugitive emissions and other emission sources can result in the potential for low-level ambient air concentrations of constituents from the two streams at locations neighboring industrial facilities where they are manufactured. Both EPA and state agencies enforce a wide range of volatile organic compound and hazardous air pollutant environmental regulations that control these emissions. 1,3-Butadiene off-property concentrations from category streams will be further reviewed nationally by EPA as the Clean Air Act Section 112f residual risk provisions are implemented. These regulations on 1,3-butadiene emissions limit the potential for emissions of the streams in this HPV Category.

Human Health

Crude Butadiene C4 streams have a low order of acute toxicity. The components of Crude Butadiene C4 streams are gaseous at normal temperature and pressure; thus, ingestion or dermal absorption of this material is unlikely. Minimal effects were observed at concentrations of 5,300 mg/m^3.

Liquid Crude Butadiene C4 (test material was cooled in a dry ice bath) did not produce dermal or ocular irritation in rabbits. Exposure to liquid crude butadiene C4 is unlikely, as the components of

the streams in this category are gases at normal temperature and pressure.

A species difference in repeated dose toxicity of crude butadiene C4 was apparent between rats and mice. Minimal effects were reported in rat repeated dose toxicity tests exposed to several Crude Butadiene C4 streams (1,3-butadiene content ranging from 10 to 99.2%). The no observable adverse effect levels were the highest concentrations tested or 17,679; 20,000; or 25,100 mg/m^3 (8,000; 9,060; or 11,365 ppm, respectively) following 90, 36, or 9 days of exposure, respectively. In contrast, mortality was observed in mice exposed to 2,761 mg/m^3 1,3-butadiene (99.2%) for 90 days. Well documented species differences in 1,3-butadiene metabolism are the likely reason for the noted differences in repeat dose toxicity. Mice produce greater amounts of toxic metabolites following 1,3-butadiene exposure than rats. Available data suggest humans metabolize 1,3-butadiene similarly to rats.

Test data demonstrate that crude butadiene C4 can produce genotoxicity. *In vitro*, crude butadiene C4 demonstrated little activity in reverse mutation assays conducted in *Salmonella typhimurium* either in the presence or absence of metabolic activation. In addition, crude butadiene C4 did not increase the number of transformed foci in C3H/10T1/2 cloned 8 mouse embryo fibroblast cells. In the mouse lymphoma assay, evidence of mutagenic activity in mouse lymphoma L5178Y cells in culture was observed in the absence of metabolic activation, but not in the presence of metabolic activation. *In vivo*, several crude butadiene streams, containing 10 to 45% 1,3-butadiene, induced micronuclei formation in rats and mice following inhalation exposure.

No reproductive or developmental toxicity was observed in rats exposed to crude butadiene during the conduct of an OECD 422 repeat dose reproductive/developmental toxicity screen. Exposures to concentrations of 20,000 mg/m^3 were without effect. Further, in a prenatal developmental toxicity study, inhalation exposure of pregnant rats to 1,3-butadiene on days 5 to 16 (inclusive) of gestation elicited no developmental toxicity at any tested concentration up to 2,210 mg/m^3. Maternal toxicity was observed at levels of 442 mg/m^3. Similar to observations of species differences in repeat dose toxicity, mice were more sensitive than rats in developmental and reproductive toxicity following exposure to 1,3-butadiene. This increased sensitivity was apparent in effects on male germ cells observed in a dominant lethal study and an assessment of sperm morphology in male mice and fetal effects observed in a prenatal developmental toxicity study.

Environment

Results of distribution modeling show that chemical constituents of streams in the Crude Butadiene C4 Category will partition primarily to the air compartment, with a negligible amount partitioning to water. In the air, these constituents have the potential to rapidly degrade through indirect photolytic processes mediated primarily by hydroxyl radicals. This is expected to be the dominant route of loss and degradation process for constituents of these streams. Aqueous photolysis and hydrolysis will not contribute to the transformation of category constituents in aquatic environments because they are either poorly or not susceptible to these reactions.

Although the biodegradability of streams in this category has not been evaluated with standard testing procedures because of their high volatility, studies have demonstrated that several category constituents can be degraded by bacteria isolated from soil and surface water samples. The results from these studies show that selected stream constituents are subject to microbial degradation. However, biodegradation is unlikely to contribute to the overall degradation of constituents from these streams because they tend to partition to the air compartment.

Due to the fact that streams in this category are gaseous at ambient temperature and pressure and expected to partition predominantly to the atmosphere, aquatic toxicity testing was not conducted. However, aquatic toxicity was assessed with a model that is based on an equation developed for neutral organic chemicals, which is a reliable estimation method for the class of chemicals in streams from this category. Calculated toxicity values for two to four day exposures suggest that

category members have the potential to produce moderate toxicity, based on an effect range of 15.35 to 40.27 mg/L for selected stream constituents.

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* Companies that are part of the Olefins Panel, but do not produce Chemical Abstracts Service registration numbers in the Crude Butadiene C4 Category.

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1 CATEGORY DESCRIPTION AND JUSTIFICATION

1.1 Category Identification

For purposes of the U.S. High Production Volume (HPV) Chemical Challenge Program (Program), the Crude Butadiene C4 Category test plan submitted in May 2000 (Olefins Panel, HPV Implementation Task Group, 2000) included four production streams and eleven Chemical Abstracts Service (CAS) registration numbers (RNs) (Table 1). The test plan identified existing data and additional data to be developed, based on an extensive technical review of the category, to adequately characterize the four streams for the HPV Program endpoints. After the additional data were developed and all data evaluated to determine whether the streams formed a cohesive category as originally envisaged, it was decided that two streams, Pyrolysis C3+ and Pyrolysis C4+, should be considered as a separate category based on compositional differences and potential effects of stream constituents not shared by all four streams. Therefore, a category summary report that characterizes the HPV Program endpoints will be prepared and submitted separately for these two streams.

The following category report summarizes HPV Program data for the C4 Crude Butadiene and Butadiene Unit Heavy Ends streams, which constitute the revised Crude Butadiene C4 Category and contain ten CAS RNs (the CAS RNs listed in Table 1 except CAS RN 68513-68-8, which was shared exclusively by the Pyrolysis C3+ and Pyrolysis C4+ streams; a second CAS RN, 64742-83-2, is also shared by the C4 Crude Butadiene stream and will be retained in the revised category).

Table 1. Production Streams, CAS RNs, and CAS RN Names in the Crude Butadiene C4 Category

Production Streams	CAS RN	CAS RN Name
C4 Crude Butadiene	68476-52-8	Hydrocarbons, C4, Ethylene-Manuf.-By-Product
	68187-60-0	Hydrocarbons, C4, Ethane-Propane-Cracked
	68955-28-2	Gases, (Petroleum), Light Steam-Cracked, Butadiene Conc.
	64742-83-2	Naphtha, (Petroleum), Light Steam Cracked
	68476-44-8	Hydrocarbons, >C3
	68956-54-7	Hydrocarbons, C4, Unsatd.
	68477-41-8	Gases, Petroleum, Extractive, C3-5, Butadiene-Butene-Rich
	25167-67-3	Butene
Butadiene Unit Heavy Ends	69103-05-5	Hydrocarbons, C4-7, Butadiene Manuf. By-Product
	68477-41-8	Gases, Petroleum, Extractive, C3-5, Butadiene-Butene-Rich
	68512-91-4	Hydrocarbons, C3-4-Rich, Petroleum Distillates
Pyrolysis C3+	64742-83-2	Naphtha, (Petroleum), Light Steam Cracked
	68513-68-8	Residues, (Petroleum), Deethanizer Tower
Pyrolysis C4+	64742-83-2	Naphtha, (Petroleum), Light Steam Cracked

Note: The CAS numbers associated with corresponding production streams are shown in the above table. The definitions found in the TSCA Chemical Substance Inventory for the CAS RNs in this category are vague with respect to composition. Therefore, it is not uncommon to find that one CAS RN is used to describe different streams (different compositions) or that two or more CAS RNs are used to describe one stream (similar composition). Pyrolysis C3+ and Pyrolysis C4+, originally included in the C4 Crude Butadiene Category, will be considered as a separate category based on compositional and other differences.

The two commercial production streams, C4 Crude Butadiene and Butadiene Unit Heavy Ends, are similar from a process and toxicology perspective. Each stream can vary in composition, not only between manufacturers but also for an individual manufacturer, depending on feedstock type and process operating conditions. Although the chemical composition of the streams can vary, the defining characteristic of the two streams is that each contains a mixture of chemicals from a reaction or separation activity in the Olefins Industry hydrocarbon processes and each contains 1,3-butadiene at a minimum concentration of approximately 10%.

The two streams in this category are composed of a complex mixture of hydrocarbons. The typical carbon (C) number distribution for these streams ranges predominantly between C3 and C5. The major stream in the category on a production volume basis is a C4 stream that contains between approximately 10 to 82% 1,3-butadiene and is referred to as "C4 Crude Butadiene". Both streams contain significant levels of C4 olefins and 1,3-butadiene in particular, which is the most biologically active constituent and the major contributor to toxicological activity. This commonality is the basis for considering the two streams as a category for purposes of the HPV Program.

The TSCA Chemical Substance Inventory definitions for the CAS RNs in this and in other categories from the Olefins Panel's HPV Program can be vague with respect to composition. Therefore, it is not uncommon that a CAS RN is correctly used to describe different streams (different compositions) or that two or more CAS RNs are used to describe one stream (similar composition or process). For this reason, the data matrix for this category was developed based on two compositionally differentiated process streams, rather than on the CAS RNs in this category.

The Crude Butadiene C4 Category streams arise from production processes associated with ethylene manufacturing (see Appendix I for a description of the ethylene and associated processes). The category stream names have changed since the test plan for this category was prepared in 2001. The change came as a result of a review and a decision by the Olefins Panel to use terminology that is more broadly applied throughout the industry. Briefly, the two process streams are:

(1) C4 Crude Butadiene stream is produced from the distillation of a liquefied portion cracked gas. This stream typically contains approximately 40 to 60% 1,3-butadiene (Table 2). However, it can contain as little as 10% or as much as 82% 1,3-butadiene. Other hydrocarbons in this stream are predominately C4. This stream was referred to as Butadiene Concentrate in the Crude Butadiene C4 Category Test Plan (Olefins Panel, HPV Implementation Task Group, 2001).

(2) Butadiene Unit Heavy Ends stream is produced from extractive distillation. This stream contains approximately 13 to 92% 1,3-butadiene (Table 2). Other hydrocarbons in this stream are predominately C4. This stream was referred to as High Butadiene Heavy Ends in the Crude Butadiene C4 Category Test Plan.

Table 2. Typical Constituent (wt%) Range in Streams of the Crude Butadiene C4 Category

Constituent	C4 Crude Butadiene Stream (wt %)	Butadiene Unit Heavy Ends Stream (wt %)
tert-Butyl Catechol	0 - 0.01	
Methanol	0.0 - 0.3	
Methylacetylene & Propadiene	0.0 - 2.3	
Ethyl- & Vinylacetylene	0.7 - 3.0	
Propylene	0.0 - 1.9	
Other C3 & Lighter Hydrocarbons	0.5 - 1.7	
Isobutane	0.4 - 22	
Isobutylene	0.5 - 29	
n-Butane	1.5 - 30	0.0 - 6.0
cis- & trans-Butene-2	3.5 - 54	5 - 50
Butene-1	2.5 - 25	0.0 - 4.0
1,3-Butadiene	10 - 82	13 - 92
1,2-Butadiene	0.0 - 1.4	0.0 - 2.0
Other C5 & Higher	0.0 - 8.0	
Vinylcyclohexene	0.0 - 1.0	
Isopentane		0.0 - 3.0
Other C8 Hydrocarbons		0.0 - 4.0

Note 1: The balance of these streams is expected to be other hydrocarbons that have boiling points in the ranges of the listed constituents.

Note 2: The ranges should not be considered to represent absolute limits for these streams. They represent the high and low reported values, and are industry typical limit values.

1.2 Purity/Impurities/Additives

A polymerization inhibitor (typically tertiarybutylcatechol, CAS RN 98-29-3, at 50 ppm) is usually added to Crude Butadiene C4 streams prior to shipment.

1.3 Physico-Chemical Properties

The two streams in this category are complex, containing many different hydrocarbons (Table 2), and can vary in composition not only between manufacturers but also for an individual manufacturer, depending on feedstock type and operating conditions. The seven constituents listed in Tables 3 and 4 comprise significant proportions of the two streams, which is why they were selected to represent the potential range of physico-chemical (PC) properties of the streams in this category. Therefore, these data can be used to adequately characterize the five PC endpoints of substances in this category for the HPV Program.

Table 3. Summary of Calculated Physico-Chemical Properties for Selected Chemicals Contained by Streams in the Crude Butadiene C4 Category

Chemical	Melting Point (°C)	Boiling Point (°C)	Vapor Pressure (hPa@ 25°C)	Log P_{ow}	Water Solubility (mg/L)
Isobutane	-132.6	3.2	3.45 E3	2.23	496.4
n-Butane	-120.3	19.6	2.41 E3	2.31	424.1
Isobutylene	-130.9	10.2	2.97 E3	2.23	495.6
cis-Butene-2	-120.4	27.8	2.31 E3	2.09	652.7
trans-Butene-2	-120.4	27.8	2.31 E3	2.09	652.7
Butene-1	-121.7	17.6	2.48 E3	2.17	557.7
1,3-Butadiene	-123.2	15.6	2.73 E3	2.03	732.4

Calculated values derived by the EPIWIN program (EPIWIN, 1999).

Table 4. Summary of Measured Physico-Chemical Properties for Selected Chemicals Contained by Streams in the Crude Butadiene C4 Category

Chemical	Melting Point (°C)	Boiling Point (°C)	Vapor Pressure (hPa@ 25°C)	Log P_{ow}	Water Solubility (mg/L)
Isobutane	-138.3	-11.7	3.08 E3	2.76	175.1
n-Butane	-138.2	-0.5	2.43 E3	2.89	135.6
Isobutylene	-140.4	-6.9	3.08 E3	2.34	399.2
cis-Butene-2	-105.5	0.8	2.33 E3	2.31	423.5
trans-Butene-2	-105.5	0.8	2.33 E3	2.33	407.1
Butene-1	-145.0	-1.3	3.00 E3	2.40	354.8
1,3-Butadiene	-108.9	-4.4	2.81 E3	1.99	792.3

Measured values from the EPIWIN experimental database (EPIWIN, 1999).

The following sections identify the values used to define the five PC endpoints of the two streams in this category.

1.3.1 Melting Point (Range)

Based on calculated values, the streams in this category can have a melting point range of -132.6 to -120.3 °C. Based on measured values, the streams in this category can have a melting point range of -145.0 to -105.5 °C. The calculated data compare favorably with the measured data. The measured data are considered the appropriate primary data set to characterize the melting point range of category members.

1.3.2 Boiling Point (Range)

Based on calculated values, the streams in this category can have a boiling point range of 3.2 to 27.8 °C. Based on measured values, the streams in this category can have a boiling point range of

-11.7 to 0.8 °C. The calculated data are not comparable with the measured data. The measured data are consistent with process knowledge and are considered the appropriate primary data set to characterize the boiling point range of category members.

1.3.3 Vapor Pressure (Range)

Based on calculated values, the streams in this category can have a vapor pressure range of 2.31 E3 to 3.45 E3 hPa at 25 °C. Based on measured values, the streams in this category can have a vapor pressure range of 2.33 E3 to 3.08 E3 hPa at 25 °C. The calculated data compare favorably with the measured data. The measured data are consistent with process knowledge and are considered the appropriate primary data set to characterize the vapor pressure range of category members.

1.3.4 Log P_{ow} (Range)

Based on calculated values, the streams in this category can have a log P_{ow} range of 2.03 to 2.31. Based on measured values, the streams in this category can have a log P_{ow} range of 1.99 to 2.89. The calculated data compare favorably with the measured data for the unsaturated molecules, 2.03 to 2.23 vs. 1.99 to 2.40, respectively. In comparison, the calculated data for the saturated molecules are not comparable with the measured data. The measured data are considered the appropriate primary data set to characterize the log P_{ow} range of category members.

1.3.5 Water Solubility (Range)

Based on calculated values, the streams in this category can have a water solubility range of 424.1 to 732.4 mg/L. Based on measured values, the streams in this category can have a water solubility range of 135.6 to 792.3 mg/L. As with the log P_{ow} data, the calculated data compare favorably with the measured data for the unsaturated molecules, 495.6 to 732.4 mg/L vs. 354.8 to 792.3 mg/L, respectively. In comparison, the calculated data for the saturated molecules are not comparable with the measured data. The measured data are considered the appropriate primary data set to characterize the water solubility range of category members.

1.4 Category Justification

Much of the data used to characterize human health endpoints of the two streams in the Crude Butadiene C4 Category are for 1,3-butadiene, which is the most chemically reactive of the constituents and hence presumed the most biologically active component and major contributor to toxicological activity. This chemical is present in the streams covered by this category at concentrations between approximately 10 to 92% (by weight). The presence of this chemical at concentrations $\geq$10% by weight presupposes that the stream would result in positive genotoxicity as the most sensitive endpoint. Supporting this presumption, two C4 Crude Butadiene stream samples, each with a different % 1,3-butadiene concentration (10 and 45%), have been shown to be genotoxic in mice.

At the time of this document's preparation, 1,3-butadiene has adequate quality data to characterize each HPV Program human health endpoint. Although an older acute inhalation toxicity study contained insufficient experimental detail to fully assess its quality, the results are consistent with the overall understanding of the hazard for this chemical. Therefore, the existing study was used to characterize the acute toxicity endpoint for 1,3-butadiene and to support the characterizaton of this category as a whole. There are also test data available for three different samples from the C4 Crude Butadiene stream. The composition of these samples was:

- 67% 1,3-butadiene; 30% butenes; 2% 1,2-butadiene; 1% other
- 45% 1,3-butadiene; 20% butanes; 30% butenes; 5% other

- 10% 1,3-butadiene; 29% 1-butene; 29% trans-2-butene; 12% cis-2-butene; 11% isobutylene; 4% n-butane; 4% isobutane; 1% other

Data for pure 1,3-butadiene together with data from two mid 1,3-butadiene-content C4 Crude Butadiene stream samples (approximately 45 and 67%) and one low 1,3-butadiene-content C4 Crude Butadiene stream sample (approximately 10%), adequately characterize the HPV Program human health effects endpoints for the two streams in this category.

2 EXPOSURE AND USE

The Crude Butadiene C4 Category contains 10 CAS RNs (Table 1) that are associated with the following two process streams:

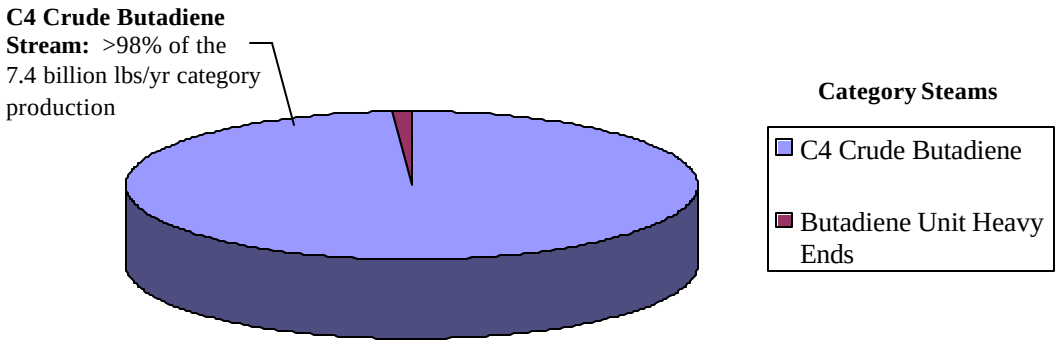
- C4 Crude Butadiene (referred to as Butadiene Concentrate in the Crude Butadiene C4 Category Test Plan)
- Butadiene Unit Heavy Ends (referred to as High Butadiene Heavy Ends in the Crude Butadiene C4 Category Test Plan)

These two streams are manufactured in ethylene production or butadiene finishing units (see Appendix II) and account for 100% of annual Crude Butadiene C4 Category production in the United States.

The C4 Crude Butadiene stream is a co-product of the ethylene manufacturing process and is processed at butadiene finishing units where it is separated into 1,3-butadiene and other 4-carbon (C4) chemicals. This stream accounts for over 98% of the 7.4 billion lbs/year (Figure 1), which was the total commercial production of streams in the Crude Butadiene C4 Category as reported by participants in the HPV Program based on their 1998 TSCA IUR reports. The balance of the category production consists of the Butadiene Unit Heavy Ends stream, which is recycled back into the production process or used as fuel in process furnaces. Subsequent processing of the streams in this category produces other substances (e.g., 1,3-butadiene) and the consumption of the original streams.

This category contains two Olefins Industry HPV streams that contain significant levels of 1,3-Butadiene (generally 10% by weight or greater). The C4 Crude Butadiene stream is transported in bulk by pipeline, barge, tank rail car, and infrequently by tank truck. There are no consumer uses of these streams and consequently no consumer exposure is expected.

Figure 1. Crude Butadiene C4 Category Production by Stream



For workers at ethylene and butadiene production plants where the streams in this category are manufactured and used, exposure to the streams is limited because processing occurs in closed systems. In addition, the Occupational Safety and Health Administration (OSHA) Butadiene Standard applies to these systems and thus limits worker exposure to the streams in this category. The Standard requires controls and work practices that limit 1,3-butadiene occupational exposure to less than 1 ppm, 8-hour TWA (time weighted average), and a short-term (15 minute) exposure of 5 ppm, which is the OSHA standard for 1,3-butadiene (OSHA, 1997). In addition, the OSHA Standard establishes an Action Level of 0.5 ppm (8-hour TWA), which effectively limits occupational exposure to 1,3-butadiene. Thus, the potential for occupational exposure to these streams is regarded to be minimal.

C4 Crude Butadiene, which accounts for approximately 98% of the production volume in the category, typically contains 50% 1,3-butadiene (reported concentrations of 1,3-butadiene in the C4 Crude Butadiene stream range from 10 to 82%). An 8-hour TWA and 15-minute STEL (Short Term Exposure Limit) occupational exposure to a typical C4 Crude Butadiene stream might approach 2 ppm and 10 ppm, respectively, for a facility complying with the OSHA 1,3-Butadiene Standard. Facilities that control below the Action Level of 0.5 ppm would have proportionally lower occupational exposures. For industrial workers at these facilities, the most likely exposure potential occurs through inhalation of low-level concentrations in air of vapors that escape from the closed process, such as fugitive emissions from valves and flanges; operations such as sampling, connecting, and disconnecting bulk transportation vessels (tank rail cars and barges); and during infrequent opening of equipment for maintenance.

Fugitive emissions and other emission sources can also result in the potential for low-level ambient air concentrations of the 2 category streams at locations neighboring the industrial facilities. Both EPA and state agencies enforce a wide range of volatile organic compound and hazardous air pollutant environmental regulations that control these emissions. Most industrial facilities (21 of 23 reporting sites) that produce or use these streams are located in the states of Texas or Louisiana. In Louisiana, the facilities are subject to an off-property 1,3-butadiene ambient air standard of 0.92 $\mu g/m^3$ (0.42 ppb) (Louisiana Department of Environmental Quality, 2003). Facilities in Texas are

subject to other requirements[1]. 1,3-Butadiene off-property concentrations resulting from category streams will be further reviewed nationally by EPA as the Clean Air Act Section 112f residual risk provisions are implemented. These regulations on 1,3-butadiene emissions limit the potential for emissions of the streams in this HPV Category.

Industrial emissions of chemicals such as 1,3-butadiene are reported annually to the EPA and made available to the public in the Toxics Release Inventory (TRI)[2]. The TRI is a publicly available EPA database that contains information on chemical releases and other waste management activities reported annually by selected industry groups as well as federal facilities. This inventory was established under the Emergency Planning and Community Right-to-Know Act of 1986 (EPCRA) and expanded by the Pollution Prevention Act of 1990.

The TRI data indicate that industrial emissions of 1,3-butadiene have significantly decreased since 1988 as production increased. 1,3-Butadiene production increased from 3.17 billion pounds in 1988 to 4.43 billion pounds in 2000 (Chemical and Engineering News; 1998, 2002). The TRI data from 2000 indicate that emissions of 1,3-butadiene declined by 69% since 1988 or from 7.7 million pounds to 2.4 million pounds per year in 2000. Similarly, Louisiana and Texas, where most of the 1,3-butadiene reporting industrial facilities are located, reported similar decreases in 1,3-butadiene TRI emissions since 1988: 69% and 67%, respectively, for total emissions and 69% and 63%, respectively, for air emissions.

The EPA National Toxics Inventory (NTI)[3] includes reported emissions of 1,3-butadiene. Emissions from streams in the Crude Butadiene C4 Category make up a part of the chemical sector's contribution to the NTI. The NTI includes emissions from major sources (e.g., chemical plants and oil refineries), area sources (e.g., gas stations), other stationary sources (e.g., wildfires and other prescribed burning), and mobile sources. Mobile sources include both on-road and off-road sources of emissions (e.g., cars, trucks, buses, off road vehicles, aircraft, locomotives, and commercial marine vessels).

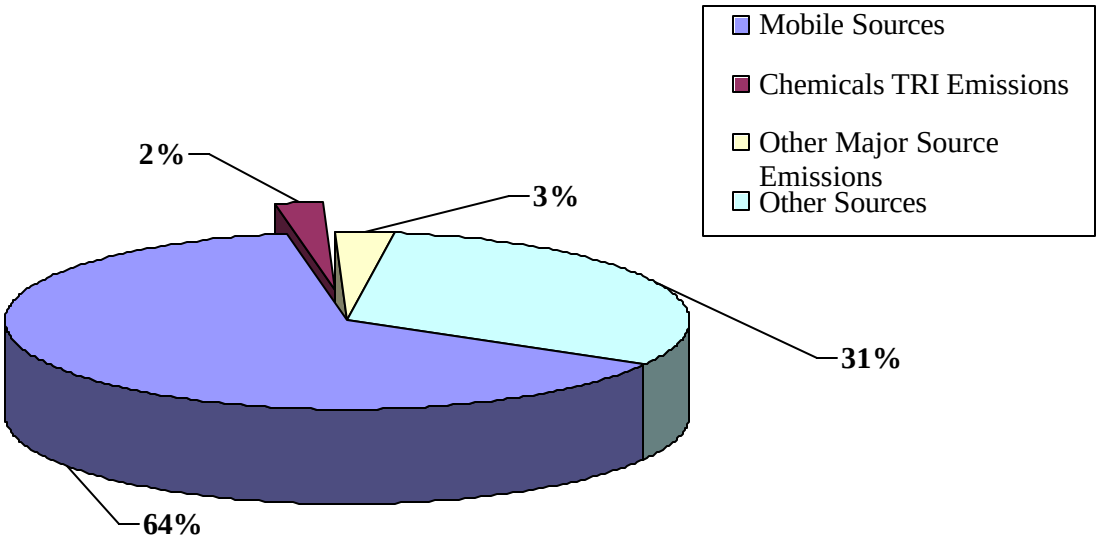
The 1996 NTI indicates total nationwide 1,3-butadiene emissions were 52,000 tons (104 million pounds). Major sources accounted for 5% of this total, mobile sources accounted for 64% and other sources made up the remaining 31%. The chemical sector's 1996 1,3-butadiene air emissions from the TRI data are a component of the NTI major source emissions, and equivalent to 2% of the total NTI emissions. These values are represented in Figure 2.

[1] 1,3-Butadiene monitoring data for Texas from the Community Air Toxics Monitoring Network can be found at: http://www.tnrcc.state.tx.us/air/monops/cat97/pdfs/97butadi13.pdf.

[2] EPA TRI website: http://www.epa.gov/tri/.

[3] Information concerning the EPA's NTI and their National Air Toxics Assessment can be found on the EPA Air Toxics website: http://www.epa.gov/ttn/atw/.

Figure 2. Percent 1,3-Butadiene Air Emissions by Source - 1996 Data



3 ENVIRONMENTAL FATE

3.1 Photodegradation

The atmosphere is the environmental compartment of interest when considering fate processes that can impact the persistence of streams in the Crude Butadiene C4 Category because they are gaseous. Results from an environmental distribution model support the assessment that chemical constituents of these streams will partition predominantly to the air compartment. The modelling results can be largely explained by the high vapor pressure of the constituents evaluated. In spite of their water solubility, wet deposition of category constituents is not likely to play a significant role in their atmospheric fate. Constituents of streams in this category have the potential to degrade at a significant rate in the atmosphere through indirect photolytic process mediated primarily by hydroxyl radicals (OH^-). In comparison, direct photolysis is not expected to contribute to the degradative fate of these streams in the aqueous environment.

3.1.1 Direct Photodegradation

The direct photolysis of an organic molecule occurs when it absorbs sufficient light energy to result in a structural transformation (Harris, 1982a). The reaction process is initiated when light energy at a specific wavelength elevates a molecule to an electronically excited state. However, the excited state is competitive with various deactivation processes that can result in the return of the molecule to a non excited state.

The absorption of light in the ultra violet (UV)-visible range, 110-750 nm, can result in the electronic excitation of an organic molecule. Light in this range contains energy of the same order of magnitude as covalent bond dissociation energies (Harris, 1982a). Higher wavelengths (e.g., infrared) result only in vibrational and rotational transitions, which do not tend to produce structural changes to a molecule.

The stratospheric ozone layer prevents UV light of less than 290 nm from reaching the earth's surface. Therefore, only light at wavelengths between 290 and 750 nm can result in photochemical

transformations in the environment (Harris, 1982a). Although the absorption of UV light in the 290-750 nm range is necessary, it is not always sufficient for a chemical to undergo photochemical degradation. Energy may be re-emitted from an excited molecule by mechanisms other than chemical transformation, resulting in no change to the parent molecule.

A conservative approach to estimating a photochemical degradation rate is to assume that degradation will occur in proportion to the amount of light at wavelengths >290 nm absorbed by the molecule (Zepp and Cline, 1977). Saturated hydrocarbons do not absorb light above 200 nm. Characteristic absorbance maxima (λ_{max}) and associated molar absorptivities (ε) for two unsaturated hydrocarbons, including 1,3-butadiene, are listed in Table 5 (Harris, 1982a).

Table 5. Characteristic Absorbance Maxima (λ_{max}) and Associated Molar Absorptivities (ε) for Two Unsaturated Hydrocarbons from Streams in the Crude Butadiene C4 Category

Hydrocarbon	λ below 290 nm	
	λ_{max*}	ε
Ethylene	193	10,000
1,3-Butadiene	217	20,900

* Values developed in organic solvents and regarded as approximate absorption maxima in aqueous solution.

Olefins with one double bond, two conjugated double bonds, or multiple un-conjugated bonds, which constitute the majority of the chemicals in the Crude Butadiene C4 Category, do not absorb appreciable light energy above 290 nm. Streams in this category do not contain constituent molecules of significant concentration that will undergo direct photolysis. Therefore, this fate process will not contribute to a measurable degradative removal of chemical constituents in this category from the environment.

3.1.2 Indirect Photodegradation

In the environment, organic chemicals emitted into the troposphere are degraded by several important transformation processes. The dominant transformation process for most compounds is the daylight reaction with hydroxyl (OH^-) radicals (Atkinson, 1988; Atkinson, 1989). The rate at which an organic compound reacts with OH^- radicals is a direct measure of its atmospheric persistence (Meylan and Howard, 1993).

AOPWIN estimates the rate constant for the atmospheric, gas-phase reaction between photochemically produced hydroxyl radicals and organic chemicals. The rate constants estimated by the program are then used to calculate atmospheric half-lives for organic compounds based upon an average atmospheric concentration of hydroxyl radicals.

Since the reactions necessary for this degradative process only take place in the presence of sunlight, the atmospheric half-lives are normalized for a 12-hour day. The seven chemicals selected to represent the atmospheric half-life range of streams in this category are C4 hydrocarbons that are predominant among the 10 CAS RNs (Table 6).

Atmospheric oxidation as a result of hydroxyl radical attack can be a significant route of degradation for streams in this category. Based on calculated values, streams in this category can have an atmospheric half-life range of 1.9 to 52.6 hours as a result of indirect photolysis by hydroxyl radical attack.

Table 6. Hydroxyl Radical Photodegradation Half-life of Selected Chemicals from Streams in the Crude Butadiene C4 Category

Chemical	Calculated Half-Life* (hrs)	OH^- Rate Constant (cm^3/molecule -sec)
Isobutane	52.6	2.4 E-12
n-Butane	48.8	2.6 E-12
Isobutylene	2.5	51.7 E-12
Cis-Butene-2	2.3	56.7 E-12
Trans-Butene-2	3.0	64.3 E-12
Butene-1	4.7	27.4 E-12
1,3-Butadiene	1.9	66.6 E-12

* Atmospheric half-life values are based on a 12-hr day and an OH^- concentration of 1.5E6, which is the default concentration used by the model.

3.2 Stability in Water (Hydrolysis)

Hydrolysis of an organic molecule occurs when a molecule (R-X) reacts with water (H_2O) to form a new carbon-oxygen bond after the carbon-X bond is cleaved (Gould, 1959; Harris, 1982b). Mechanistically, this reaction is referred to as a nucleophilic substitution reaction, where X is the leaving group being replaced by the incoming nucleophilic oxygen from the water molecule. The leaving group, X, must be a molecule other than carbon because for hydrolysis to occur, the R-X bond cannot be a carbon-carbon bond.

The carbon atom lacks sufficient electronegativity to be a good leaving group and carbon-carbon bonds are too stable (high bond energy) to be cleaved by nucleophilic substitution. Thus, hydrocarbons, including alkenes, are not subject to hydrolysis (Harris, 1982b) and this fate process will not contribute to the degradative loss of chemical constituents in this category from the environment.

Under strongly acidic conditions the carbon-carbon double bond found in alkenes, such as those in the Crude Butadiene C4 Category, will react with water by an addition reaction mechanism (Gould, 1959). The reaction product is an alcohol. This reaction is not considered to be hydrolysis because the carbon-carbon linkage is not cleaved and because the reaction is freely reversible (Harris, 1982b).

Chemicals that have a potential to hydrolyze include alkyl halides, amides, carbamates, carboxylic acid esters and lactones, epoxides, phosphate esters, and sulfonic acid esters (Neely, 1985). The chemicals in this category are primarily olefins that contain at least one double bond (alkenes). The majority of the remaining chemicals are saturated hydrocarbons (alkanes). These two groups of chemicals contain only carbon and hydrogen. As such, their molecular structure is not subject to the hydrolytic mechanism described above. Therefore, chemicals in the Crude Butadiene C4 Category have a very low potential to hydrolyze, and this degradative process will not contribute to their removal in the environment.

3.3 Distribution in the Environment

Fugacity-based multimedia modeling provides basic information on the relative distribution of a chemical between selected environmental compartments, which can include air, soil, water, sediment, suspended sediment, and biota. A widely used fugacity model, the EQC (Equilibrium Criterion) Level I model (Mackay *et al.*, 1996; Mackay, 1998) calculates chemical distribution between these compartments based on the input of basic physicochemical parameters including

molecular weight, water solubility, log P_{ow}, and melting point.

Results of the EQC Level I model (Table 7) for selected chemical constituents of streams from this category suggest that they will partition primarily to air, with a small percentage partitioning to water. These results can be explained by their high vapor pressure. Distribution of these chemicals to each remaining compartment (soil, sediment, suspended sediment, biota) is calculated as less than 0.01%.

The seven chemicals selected to characterize the transport/distribution range are C4 hydrocarbons that are predominant across the streams in this category. Physical property data (Table 4) used in the model are from the EPIWIN (1999) database.

Table 7. Environmental Distribution as Calculated by the EQC Level I Fugacity Model for Selected Chemicals from Streams in the Crude Butadiene C4 Category

Chemical	Distribution Per Environmental Compartment (%)					
	Air	Water	Soil	Sediment	Suspended Sediment	Biota
Isobutane	99.99	0.01	<0.01	<0.01	<0.01	<0.01
n-Butane	99.99	0.01	<0.01	<0.01	<0.01	<0.01
Isobutylene	99.99	0.01	<0.01	<0.01	<0.01	<0.01
cis-Butene-2	99.98	0.02	<0.01	<0.01	<0.01	<0.01
trans-Butene-2	99.98	0.02	<0.01	<0.01	<0.01	<0.01
Butene-1	99.99	0.01	<0.01	<0.01	<0.01	<0.01
1,3-Butadiene	99.97	0.03	<0.01	<0.01	<0.01	<0.01

Note: The distribution values were determined using physical property data from the EPIWIN (1999) database.

3.4 Biodegradation

Biodegradation is the use of a chemical by microorganisms as a source of energy and carbon. The parent chemical is broken down to simpler, smaller chemicals, which can be eventually converted to inorganic forms such as carbon dioxide, nitrate, sulfate, and water, depending on the composition of the parent chemical.

The microbial metabolism of aliphatic alkenes can be initiated by attack at the double bond (Watkinson and Morgan, 1990). Four degradative processes have been identified:

- Oxygenase attack upon a terminal methyl group to the corresponding alcohol, aldehyde, and acid
- Subterminal carbon oxygenase attack to the corresponding alcohol and ketone
- Oxidation across the double bond to the corresponding epoxide
- Oxidation across the double bond to the corresponding diol

Streams in the Crude Butadiene C4 Category are gaseous hydrocarbons, composed predominantly of chemicals with carbon numbers smaller than C5.

Constituent chemicals from the two process streams in this category are simple hydrocarbons (Table 2), the majority of which are calculated to partition primarily to the air where physical processes will contribute to their rapid degradation (see Indirect Photodegradation above for specific degradation rates of selected chemicals from this category). Consequently, their availability to microbial degraders can be significantly limited. Because of the partitioning behavior of

chemicals in this category, biodegradative processes will be less likely to contribute to their loss from the environment.

Streams from the Crude Butadiene C4 Category do not lend themselves to being evaluated for biodegradability using standard experimental designs because of their physical state. However, there is microbial metabolism information for several of the unsaturated C4 constituents in this category, including 1,3-butadiene, that demonstrates they have the potential to biodegrade. The sections immediately below summarize results of studies for selected constituents from this category. The data do not allow for an estimation of the extent of biodegradability relative to a standard 28-day test procedure using a microbial inoculum from a wastewater treatment facility. However, the constituents discussed below are predicted by BIOWIN, Biodegradation Probability Program (EPIWIN, 1999), as having the potential to biodegrade rapidly. [BIOWIN is a model in EPIWIN that calculates the probability of an organic chemical to rapidly biodegrade by a mixed population of microorganisms. BIOWIN can also estimate the time required to meet primary and ultimate biodegradation criteria.]

3.4.1 Propylene Biodegradation

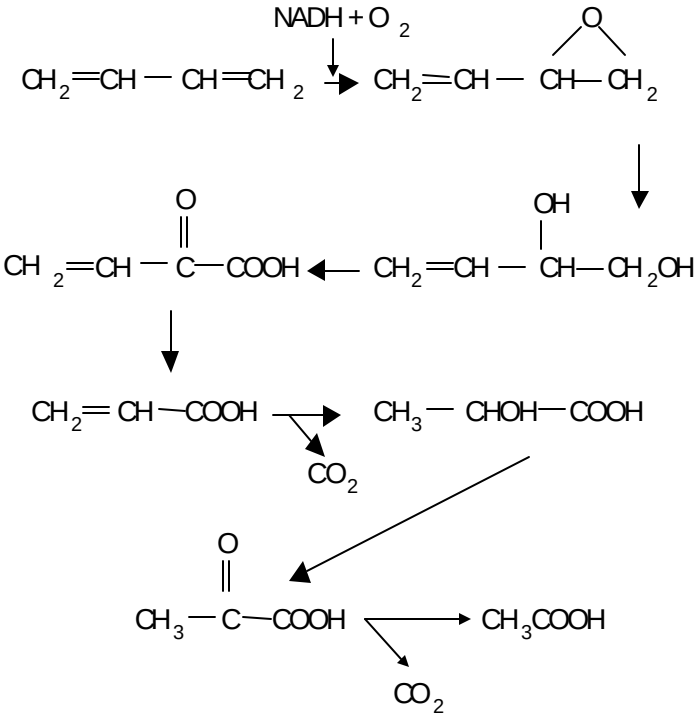
Propylene has been shown to be a growth substrate for several microorganisms. Isolated bacterial strains studied for their potential to biodegrade propylene under aerobic conditions were identified from the genus *Nocardia*, *Mycobacterium*, and *Xanthobacter* (de Bont *et al.*, 1980; de Bont *et al.*, 1982; de Bont *et al.*, 1983; van Ginkel and de Bont, 1986). Other species from the genus *Pseudomonas* and *Aerobacter* that were isolated from soil have also been associated with the ability to aerobically degrade propylene after they were shown to metabolize propylene oxide (Raja, 1991), an intermediate in the propylene metabolic pathway (van Agteren *et al.*, 1998).

Two pathways for the aerobic metabolism of propylene have been described (van Agteren *et al.*, 1998) that include the formation of either 1,2-propanediol or acetyl CoA prior to mineralization to CO_2.

3.4.2 1,3-Butadiene Biodegradation

Experimental studies to determine a catabolic pathway for 1,3-butadiene as mediated by a *Nocardia sp*. (Watkinson and Somerville, 1976) resulted in the series of reactions shown in Figure 3.

Figure 3. Proposed Microbial Metabolic Pathway for the Degradation of 1,3-Butadiene by a *Nocardia sp.*



The intermediary metabolic steps depicted in Figure 3 result in the production of acetic acid (CH_3COOH) which can be further metabolized. In addition, 1,3-butadiene has been estimated to have an aerobic aquatic biodegradation half-life ranging from 1 to 4 weeks (Howard *et al.,* 1991).

3.4.3 1-Butene Biodegradation

Isolated bacterial strains have been evaluated for their potential to biodegrade 1-butene under aerobic conditions. Bacteria from two genus, *Mycobacterium spp.* and *Xanthobacter spp.*, isolated from environmental samples have demonstrated the ability to degrade 1-butene (Hou *et al.*, 1983; Habets-Crützen *et al*., 1984; van Ginkel and de Bont, 1986; Weijers *et al*., 1995). Epoxybutane was shown to be converted to the corresponding ketone using a cell extract from a *Xanthobacter* spp. (Weijers *et al.*, 1995). These studies suggest that 1-butene can be biodegraded and that microbial metabolism can contribute to the overall loss of this chemical from the environment.

3.4.4 2-Butene Biodegradation

Although 2-butene has not been reported as a microbial growth substrate, an isolated bacterial strain, *Xanthobacter spp*., was evaluated for its potential to biodegrade various epoxyalkanes. Both diastereomeric forms of 2,3-expoxybutane were shown to degrade with degradation rates of 6 and 9 nmol/min/mg protein for trans- and cis- geometric isomers, respectively (Weijers *et al.*, 1988). These data suggest that a metabolic pathway is present in bacteria that will degrade these alkenes.

3.4.5 Isobutylene Biodegradation

Although isobutylene has not been reported as a growth substrate for bacteria, isolated bacterial strains have been evaluated for their potential to biodegrade 1-butene under aerobic conditions. Epoxybutane was shown to be converted to the corresponding ketone using a cell extract from a *Xanthobacter spp*.(Weijers *et al.*, 1995). In the same study, 2-methyl-1,2-epoxypropane was not converted suggesting that isobutylene metabolism is not mediated in a manner similar to 1-butene

by this organism. However, because of the structural similarity between 1-butene and isobutylene, isobutylene biodegradation may occur through a process not yet evaluated.

3.4.6 Abiotic and Biotic Degradation Summary

The stream constituents from this category will partition primarily to the air where physical degradative processes will dominate their fate. Data show that these chemicals are subject to rapid physical degradation. Selected constituents have also been shown to be subject to biodegradation. Overall, the constituent chemicals and consequently the streams from this category are expected to degrade rapidly in the environment from physical processes and not persist.

4 HUMAN HEALTH HAZARDS

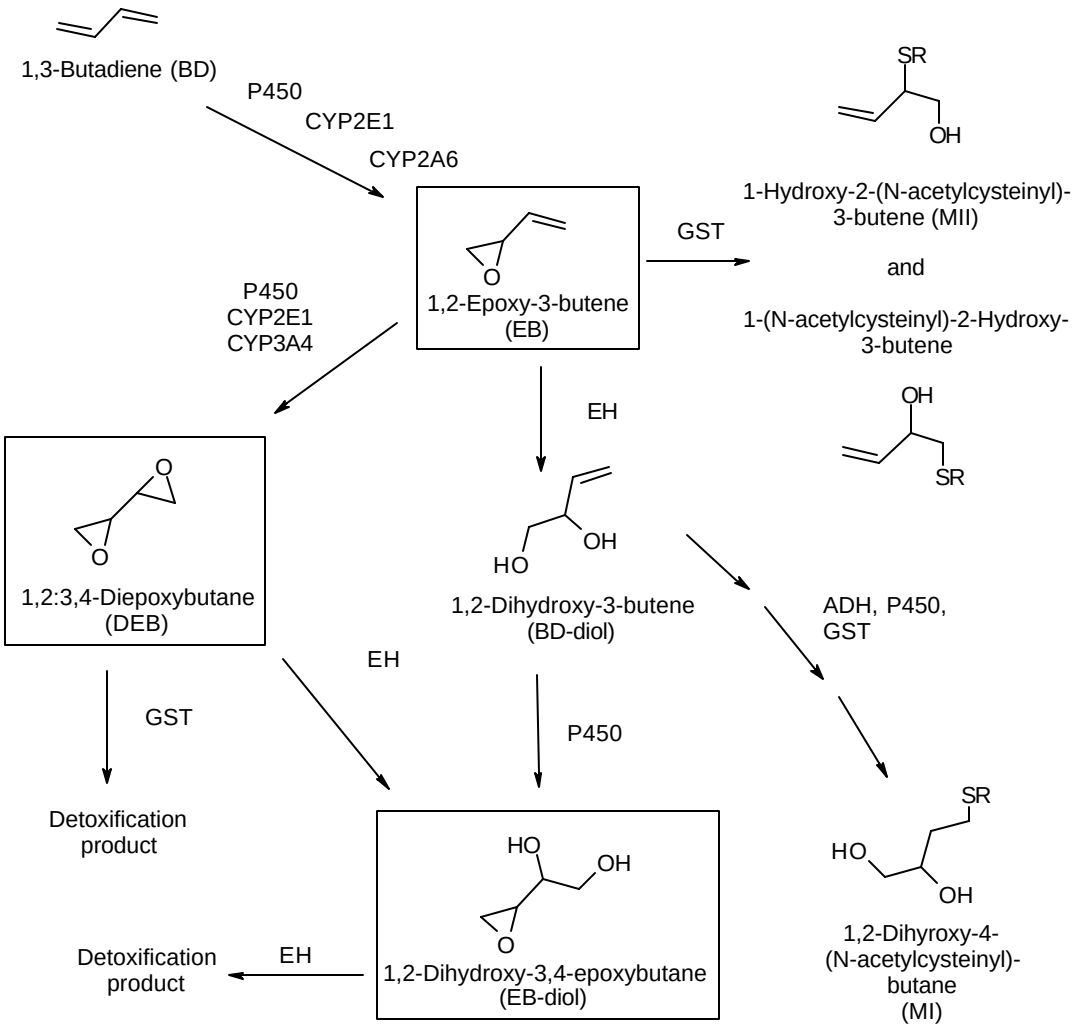
The two streams that comprise the Crude Butadiene C4 Category, which together contain ten CAS RNs, vary in 1,3-butadiene content, ranging from 10 to 92% 1,3-butadiene. Much of the data used to characterize the streams in this category are for 1,3-butadiene, which is the most biologically active constituent and thus the major contributor to toxicological activity. Therefore, data collected on 1,3-butadiene are included in the summaries below. The presence of this chemical at concentrations $\geq$10% by weight presupposes that the stream would result in positive genotoxicity as the most sensitive endpoint. Supporting this presumption, two samples from the Crude Butadiene C4 stream, containing 10 and 45% 1,3-butadiene, have been shown to be genotoxic. Data for pure 1,3-butadiene together with data from a mid 1,3-butadiene (approximately 45 to 67%) and a low 1,3-butadiene (approximately 10%) stream adequately characterize the HPV Program human health effects endpoints for the streams in this category.

4.1 Effects on Human Health

4.1.1 Toxicokinetics, Metabolism, and Distribution

1,3-Butadiene is initially oxidized to 1,2-epoxy-3-butene (EB), a reaction mediated primarily by P450 CYP 2E1 (Csanady *et al*., 1992; Duescher and Elfarra, 1994) (Figure 4). Further oxidation of EB produces 1,2:3,4-diepoxybutane (DEB) (Seaton *et al.*, 1995). Detoxification of EB proceeds by conjugation, mediated by glutathione-S-transferase (GST), or by hydrolysis, mediated by epoxide hydrolase (EH). Hydrolysis produces the 1,2-dihydroxy-3-butene (BD-diol) metabolite. Both DEB and BD-diol undergo further conversions *in vivo*, the former by EH mediated hydrolysis and the latter by P450 mediated oxidation, to produce the 1,2-dihydroxy-3,4-epoxybutane metabolite, known also as butadiene diol-epoxide (EB-diol) (reviewed in Himmelstein *et al.*, 1997). BD-diol can also be metabolized by P450 to hydroxymethylvinylketone (HMVK) (Kemper *et al.*, 1998), which may form $1N^2$-propanodeoxyguanosine DNA adducts *in vitro*. (Powley *et al*., 2003). EB, DEB, EB-diol, and HMVK are reactive electrophilic compounds with the potential to form carcinogenic intermediates from 1,3-butadiene metabolism *in vivo*.

Figure 4. Partial metabolic scheme for 1,3-butadiene (taken from Albertini *et al.*, 2003).



Direct GST mediated conjugation of EB with glutathione (GSH) leads to two detoxification products. One of these (i.e., 1-hydroxy-2-(N-acetylcysteinyl)-3-butene, also known as the urinary MII compound), as an isomeric mixture with 1-(N-acetylcysteinyl)-2-hydroxy-3-butene, is a biomarker of the conjugation detoxification pathway. GST mediated conjugation of HMVK with GSH leads to the production of 1,2-dihydroxy-4-(N-acetylcysteinyl)-butane (also known as the urinary MI compound). MI is a biomarker of the hydrolytic pathway because this detoxification pathway for EB is mediated initially by EH. The ratio MI/(MI + MII) in urine defines the relative importance of hydrolysis vs. conjugation in detoxification of EB (Bechtold *et al.*, 1994; reviewed in Henderson *et al.*, 1996).

In vitro studies have shown that mice are 2- and 10-fold more efficient than rats in oxidizing 1,3-butadiene to EB (Schmidt and Loeser, 1985; Csanady *et al.*, 1992). Furthermore, the second oxidation step to DEB could be mediated *in vitro* only by mouse liver microsomes (Csanady *et al.*, 1992). *In vivo* studies of 1,3-butadiene metabolism in mice and rats have also shown large inter-species differences. MI/(MI + MII) ratios in urine for mice and rats exposed to 1,3-butadiene by inhalation indicate that conjugation detoxification predominates in mice but that hydrolysis is more important in rats (Henderson *et al.*, 1996).

In summary, mice are more efficient in oxidation of 1,3-butadiene to electrophilic metabolites (especially to DEB), while rats are more efficient in hydrolytic detoxification. The existing metabolism data suggest that metabolism in humans appears to be more like metabolism in rats than in mice.

4.1.2 Acute Toxicity

Data are available to evaluate acute toxicity of streams in the Crude Butadiene C4 Category. As the streams are gaseous at room temperature, data are from inhalation toxicity studies (Table 8).

Table 8. Summary of Acute Inhalation Toxicity Data

CAS RN and Stream/Chemical Name (% 1,3-Butadiene)	Test Organism	Exposure Duration (hr)	LC_{50} (mg/m^3)
68955-28-2 C4 Crude Butadiene (45)	Rat	4	5,300
106-99-0 1,3-Butadiene (>99)	Rat	4	285,000
106-99-0 1,3-Butadiene (>99)	Mouse	2	270,000

Inhalation

Studies in Animals

Rats (5/sex) were exposed to 5,300 mg/m^3 of butadiene concentrate (CAS # 68955-28-2: 45% 1,3-butadiene; 20% butanes; and 30% butenes) in air for four hours (Gulf Oil Chemical Co., 1985). Clinical observations and body weights were recorded for fourteen days following exposure. No mortality was observed at this concentration and all rats appeared normal on days 2 to 14. Clinical observations included respiratory sounds in 2 male rats post exposure and minimal porphyrin around the eyes in one female rat. Necropsy revealed one female rat with an ovary filled with red fluid. The LC_{50} was >5,300 mg/m^3.

In a poorly reported study, LC_{50} values for 1,3-butadiene were determined to be 285,000 mg/m^3 (129,000 ppm) and 270,000 mg/m^3 (122,000 ppm) for rats (4 hr) and mice (2 hr), respectively (Shugaev, 1969).

Conclusion

Available data adequately address the acute toxicity of the Crude Butadiene C4 Category for the relevant route of inhalation exposure. Streams in this category are gaseous at room temperature. Acute inhalation toxicity tests have been conducted for streams containing either 45 or 100% 1,3-butadiene. No toxicity was observed for exposures up to 5,300 mg/m^3.

4.1.3 Irritation

Skin and eye irritation of Crude Butadiene C4 Category has been examined in rabbits.

Skin Irritation

Studies in Animals

In an irritation screening study, 0.1 ml of butadiene concentrate (CAS# 68955-28-2: 67% 1,3-butadiene; 30% butenes; and 2% 1,2-butadiene) was applied to the skin of one male and one female

New Zealand White rabbit (Mobil Environmental and Health Science Laboratory, 1985). The application site was occluded with a rubber dam. No irritation was observed at 1, 3, or 7 days after dosing.

Eye Irritation

Studies in Animals

In an irritation screening study, 0.1 ml of butadiene concentrate (CAS# 68955-28-2: 67% 1,3-butadiene; 30% butenes; and 2% 1,2-butadiene) was applied to the eye of one male and one female rabbit (Mobil Environmental and Health Science Laboratory, 1985a). Test stream was stored on dry ice prior to administration. No irritation was observed at 1, 3, or 7 days after dosing.

Conclusion

Butadiene concentrate is nonirritating to rabbit skin and eyes. Lack of irritation may be due to non irritating properties of the test stream or rapid removal of test stream from the application site by evaporation.

4.1.4 Repeated Dose Toxicity

Repeated dose toxicity tests have been conducted on a variety of streams in this category (Table 9). These studies range from 9 to 98 days in duration and have been conducted in rats and mice.

Table 9. Summary of Repeated Dose Toxicity Data

CAS RN and Stream Name (% 1,3-Butadiene)	Test Organism	Exposure Duration (days)	NOAEL (mg/m^3)
68476-52-8 C4 Crude Butadiene (10)	Crl:CD Rat	36	>20,000
106-99-0 1,3-Butadiene (>99)	CD Rat	91	>17,679
68955-28-2 C4 Crude Butadiene (45)	Fischer 344 Rat	9	>25,100
106-99-0 1,3-Butadiene (>99)	B6C3F1 Mouse	98	>2,760

Inhalation

Studies in Animals

Effects of repeated exposure to C4 Crude Butadiene (CAS# 68476-52-8: 10% 1,3-butadiene; 4% isobutane; 29% trans-2-butene; 29% 1-butene; 11% isobutylene; and 12% cis-2-butene) were evaluated as part of an OECD 422, Repeated Exposure Reproductive/Developmental Toxicity Screen in Crl:CD rats (Carney *et al.*, 2001). Twelve male and female rats were exposed to vapor concentrations 0; 2,000; 10,000; or 20,000 mg/m^3 Crude Butadiene for 36 or 37 days, 6 hr/da, 7 da/wk (this study contained an additional group of twelve female rats for reproductive and developmental toxicity screening evaluation). Males and females were sacrificed at the end of exposure. Effects on general toxicity, neurobehavioral activity, clinical chemistry, and hematology were evaluated. At necropsy, organs were weighed, evaluated grossly and histopathological evaluation was conducted. No deaths or treatment related clinical observations were reported. No treatment related changes were observed in body weight, sensory evaluation, rectal temperature,

fore/hindlimb grip performance, motor activity total counts, hematology, prothrombin time, clinical chemistry, organ weights, gross pathology, or histopathology. In evaluation of motor activity, the treatment-by-time by epoch interaction was significant. However, further evaluation indicated that this difference could be attributed to the time by epoch interaction rather than a treatment related effect. Females in the 2,000 mg/m^3 dose group had an increased hematocrit and a decrease in serum protein. However, these effects did not demonstrate a dose response and were not observed in males at the same dose level. As such these findings were considered incidental and not indicative of a treatment related response. The NOAEL in this study was 20,000 mg/m^3.

In a ninety-day repeat dose study, groups of 40 male and 40 female CD rats were exposed to 0; 2,209; 4,417; 8,334; or 17,679 mg/m^3 (0; 1,000; 2,000; 4,000; or 8,000 ppm, respectively) 1,3-butadiene (>99.2%, containing 120 ppm t-butyl catechol). Exposures were conducted for 6 hr/da, 5 da/wk for 13 weeks (Crouch *et al.*, 1979). Interim sacrifices of 10 rats/sex/group were conducted at 2 and 6 weeks, with blood being collected from all rats at these intervals and at terminal sacrifice. Body weights and food consumption were recorded weekly. Brain cholinesterase activity was determined in 5 rats/sex/group at the 2 and 6 week sacrifices and all rats at terminal sacrifice. Urine samples were collected from rats 1 to 2 weeks prior to sacrifice. Organ weights were determined for select organs with histopathology conducted on control and high exposure animals. Increased salivation was observed in female rats following 8 weeks of exposure. Decreased grooming was observed in male rats following ten weeks of exposure. Slight, non significant, reductions in body weight were observed in male rats. Organ weight and organ to brain weight ratios showed some scattered statistically significant differences among the groups but did not follow any consistent dose response trend. The NOAEL in this study was determined to be 17,679 mg/m^3.

No adverse effects were observed in rats following exposure to butadiene feedstock (CAS # 68955-28-2: 45% 1,3-butadiene; 20% butanes; and 30% butenes) in a well conducted short term repeated exposure study (Gulf Oil Chemicals Co., 1983a). Five male and five female Fischer 344 rats were exposed to 0; 2,500; or 25,100 mg/m^3 butadiene feedstock 6 hr/da, for a total of 9 days. Evaluations include body weight measurement, gross necropsy, organ weights, histopathology on selected organs, hematology, and clinical chemistry. With the exception of nasal discharge, no exposure related changes were observed. The NOAEL in this study was determined to be 25,100 mg/m^3.

Groups of 10 B6C3F1 mice/sex/group were exposed to 0; 1,380; 2,761; 5,522; 11,040; or 17,670 mg/m^3 (0; 625; 1,250; 2,500; 5,000; or 8,000 ppm, respectively) 1,3-butadiene (98.94% with 0.02% t-butyl catechol) 6 hr/da, 5 da/wk for 14 weeks (National Toxicology Program, 1984). Limited observations were conducted and included mortality and morbidity, body weight changes, gross pathology, and histolopathology on high dose and control animals. Mortality was observed in the 2,761 mg/m^3 group (1/10 males) and higher concentrations. Body weights were decreased at 5,522 mg/m^3 and higher concentrations. Despite mortality present at this concentration, the NOAEL was determined to be 2,761 mg/m^3.

Conclusion

Data are available to adequately characterize the repeated dose toxicity of Crude Butadiene C4 Category. The available studies were conducted by inhalation, the most appropriate route of exposure. Available studies cover a wide range of 1,3-butadiene concentrations (10 to 99%) in the test streams. The data are consistent in that they demonstrate minimal effects in rats with the exception of body weight changes following repeated inhalation exposures.

4.1.5 Mutagenicity

Genetic toxicity of crude butadiene has been evaluated both *in vitro* and *in vivo*. *In vitro* assays include Ames *Salmonella* Reverse Mutation assay, unscheduled DNA synthesis in rat hepatocytes, mammalian cell transformation assay, and mouse lymphoma assay. Potential for the *in vivo*

induction of chromosomal aberrations has been examined in rats and mice following inhalation exposure.

In vitro Studies

Studies in Animals

Mutagenic activity of 1,3-butadiene (CAS # 106-99-0) was evaluated in the Ames *Salmonella* Reverse Mutation assay (Arce *et al*., 1990). *Salmonella typhimurium* tester strains TA 97, TA 98, TA 100, and TA 1535 were overlaid on agar with or without mouse, rat, or human S9 activation systems in specially designed treatment chambers. 1,3-Butadiene gas was metered into the chambers at concentrations of 0, 30, 40, 50, and 60% for a 48-hour exposure period. An increase (just over 2-fold) in revertant colonies was observed only with the TA 1535 strain, all other strains demonstrated no increase. In this bacterial strain, mouse S9 had slightly higher activity than the uninduced rat or human S9 at 30% 1,3-butadiene in air. At concentrations greater than 30%, the number of revertants decreased in the presence of rat or human S9. Presence of human S9 did not substantially increase the number revertants compared to non S9 activated samples. Arochlor 1254 induced rat liver S9 fractions produced the same number of revertants as untreated mouse liver S9. Increasing the amount of rat S9 protein/plate slightly increased the number of revertants/plate without Arochlor 1254 induction, but did not produce an increase with Arochlor 1254 induction. In summary, 1,3-butadiene demonstrated weak mutagenic activity in this test system.

Butadiene concentrate (CAS # 68955-28-2: 67% 1,3-butadiene; 30% butenes; and 2% 1,2-butadiene) was evaluated for mutagenicity in the Ames *Salmonella* Reverse Mutation assay (Mobil Environmental and Health Sciences Laboratory, 1985b). Five strains of *Salmonella typhimurium* (TA 98, TA 100, TA 1535, TA 1537, and TA 1538) were incubated with 25, 50, 75, or 100 µl crude butadiene with and without Arochlor 1254 rat liver S9 activating system. Reversion frequencies in treated groups with and without S9 activation were similar to controls. The test stream was judged to be non mutagenic.

Butadiene concentrate (CAS# 68955-28-2: 45% 1,3-butadiene; 20% butanes; and 30% butenes), did not induce cell transformations in BALB/3T3-A31-1-1 cells treated *in vitro* with up to 20,000,000 mg/m^3 of the test stream (Gulf Oil Chemicals Co., 1983b). An increase in mutant frequency was observed in the mouse lymphoma cells following exposure to butadiene concentrate (CAS# 68955-28-2: 67% 1,3-butadiene; 30% butenes; and 1.2% 1,2-butadiene) in the absence of S9 activation. No increase was observed in the presence of S9 activating system (Mobil Environmental and Health Sciences Laboratory, 1985c). Unscheduled DNA synthesis (UDS) was observed in primary rat hepatocytes at 20,000,000 mg/m^3 butadiene concentrate (CAS# 68955-28-2: 45% 1,3-butadiene; 20% butanes; and 30% butenes), a level where marked cytotoxicity was observed (Gulf Oil Chemicals Co., 1984a) potentially confounding the data. No UDS was observed at treatment levels less than or equal to 10,000,000 mg/m^3.

In vivo Studies

Studies in Animals

Six male and female B6C3F1 mice were exposed to concentration of 500, 10,000, or 20,000 mg/m^3 C4 crude butadiene (CAS #, 68476-52-8: 10% 1,3-butadiene; 4% isobutane; 4% n-butane; 29% trans-2-butene; 29% 1-butene; 11% isobutylene; and 12% cis-2-butene) by inhalation for two days, 4 hr/day (Spencer *et al.*, 2001). Twenty-four hours following the final exposure, femoral bone marrow was collected to evaluate micronuclei formation in polychromatic erythrocytes. Cyclophosphamide was used as the positive control. Increases in the frequencies of micronuclei were observed in all groups treated with test material. Although a statistically significant dose

response was indicated, the difference between the low and high dose groups was minimal. Crude butadiene was positive for induction of micronuclei in this test system.

Twenty female CB6F1 mice and ten male Wistar rats were exposed to 0, 50, 200, or 500 ppm 1,3-butadiene for 5 days, 6 h/da by inhalation (Autio *et al.*, 1994). One day following exposure, smears of blood and bone marrow erythrocytes were prepared and stained. In rats, toxicity in bone marrow cells was observed in the 500 ppm exposure group. In rats, no increase in micronuclei frequencies were observed in either peripheral blood or bone marrow erythrocytes. In mice, a clear dose-dependent increase in micronuclei formation was observed in blood and bone marrow at all exposure levels tested.

Male and female Crl:CD-1 BR Swiss mice were exposed to 0; 10,780; 20,671; or 35,430 ppm butadiene concentrate (CAS # 68955-28-2: 45% 1,3-butadiene; 20% butanes; and 30% butenes) via inhalation for 2 hr/da for 2 consecutive days (Gulf Oil Chemicals Co., 1984b). Five mice per sex per dose were sacrificed on day 3 and day 4 (24 and 48 hours post-exposure), and bone marrow smears prepared. Loss of consciousness was observed in mice during exposures; no other adverse effects were observed. An increased incidence of micronuclei formation was observed at all dose levels on day three and at the two highest dose levels on day 4. Male mice exhibited an increase in micronuclei formation at the highest dose on both days.

Conclusion

Adequate data are available to evaluate the genotoxicity of crude butadiene C4. These data examine streams with a range of 1,3-butadiene content (10 to 99%). This range of 1,3-butadiene has been tested *in vitro* and *in vivo* test systems. *In vitro* studies indicate a weak mutagenic activity. *In vivo* studies demonstrate a genotoxic response from exposure to streams in this category.

4.1.6 Carcinogenicity

Inhalation

In vivo Studies in Animals

Male and female Sprague-Dawley rats were exposed to 0; 1,000; or 8,000 ppm 1,3-butadiene, 6 hr/day, 5 days/week for 111 weeks. Survival of both sexes was reduced at the high exposure level. An increase in incidence and number of animals with mammary tumors was observed in female rats at both the 1,000 and 8,000 ppm exposure levels. Increased incidences of thyroid gland adenomas and carcinomas, uterine sarcomas and Zymbal gland tumors were observed in female rats. The incidence of uterine sarcomas and Zymbal gland tumors were within the historical control range for these tumor types and may not have been related to treatment. An increased incidence in exocrine pancreas adenomas was observed in male rats at 8,000 ppm. An exposure related increase in Leydig cell tumors was observed in male rats at both concentrations.

Two cancer bioassays have been conducted in B6C3F1 mice. In the first study, male and female mice were exposed to concentrations of 0; 625; or 1,250 ppm butadiene for 61 weeks, at which time the study was canceled due to poor survivability (NTP, 1984). Numerous tumor sites were observed in both sexes. A dose-related increase in lymphomas, cardiac hemangiosarcomas and lung tumors was observed in both sexes. Increased incidence of papillomas or carcinomas of the forestomach, hepatocellular adenomas or carcinomas, ovarian granulosa cell tumors, acinar cell carcinomas of the mammary gland, brain gliomas, and Zymbal cell carcinomas were observed in one or both sexes.

Due to the poor survival rate in the initial study, a second study was conducted where B6C3F1 mice were exposed to 0, 6.25, 20, 62.5, 200 or 625 ppm 1,3-butadiene, 6 hrs/day, 5 days/week, for two years (NTP, 1993). Survival was reduced at exposure concentrations of 20 ppm and above. Tumors

were observed at numerous sites including lymphocytic lymphomas, histiocytic sarcomas, cardiac hemangiosarcomas, Harderian gland adenomas and carcinomas, hepatocellular adenomas and carcinomas, alveolar /bronchiolar adenomas and carcinomas, mammary gland adenoacanthomas and carcinomas, ovarian granulosa cell tumors and forestomach squamous cell papillomas and carcinomas. Alveolar/bronchiolar tumors were observed at the lowest dose administered in females (6.25 ppm).

Studies in Humans

Two large cohort studies provide the most definitive assessment of the relationship between cancer and butadiene exposure. One study was conducted on butadiene exposed workers in the synthetic rubber industry. Butadiene exposed workers in the butadiene monomer industry were evaluated in the second.

Delzell *et al.* (1996) evaluated mortality in a cohort of over 13,000 men employed at 8 different styrene-butadiene rubber (SBR) plants. The overall SMR for leukemia was 1.31 (95% CI = 0.97-1.74). Leukemia risks were concentrated among long-term workers with long latency working in jobs with the potential for high exposures to styrene and 1,3-butadiene. Greater than 2-fold increased leukemia risk occurred among hourly workers with more than 10 years employment and 20 years since hire and among workers in areas where there were potentially high exposures to 1,3-butadiene or styrene (e.g., polymerization, maintenance labor, laboratories). Overall about 75% of the cohort were exposed to 1,3-butadiene and 83% to styrene. In this same cohort of SBR workers, Delzell *et al.* (2001) evaluated the relationships between leukemia and exposure to 1,3-butadiene, styrene and dimethyldithiocarbamate (DMDTC). Past exposures to 1,3-butadiene, styrene and DMDTC were reconstructed through the use of exposure measurements and exposure modeling. In this analysis, leukemia mortality was significantly associated with cumulative 1,3-butadiene exposure, particularly for high ppm-years exposure levels. A stronger association was observed for cumulative 1,3-butadiene exposures with peak levels greater than 100 ppm. When concurrent exposure to styrene and DMDTC were considered, the effect of 1,3-butadiene exposure was reduced, but the exposure-response trend and apparent threshold remained. It was difficult to determine an independent effect of 1,3-butadiene exposure because of the high correlation of 1,3-butadiene exposure with styrene and DMDTC exposures. The strengths of this study are the large size, long follow-up and quantitative estimate of exposure. The weakness of this study is the concomitant exposures to styrene and DMDTC and uncertainty in the effects of 1,3-butadiene alone.

Divine and Hartman (2001) evaluated a cohort of almost 2,800 men employed at a 1,3-butadiene monomer producing plant. There were 18 cases of leukemia with an overall SMR of 1.29 (CI_{95} = 0.77 to 2.04) and all employed before 1950. The risk of leukemia decreased slightly among workers employed greater than 5 years compared to workers with less than 5-years employment in the high exposure group. This result was considered to be inconsistent with a dose-response effect. Over half the leukemia deaths occurred over 40-years since hire, which is considered an unusually long latency for leukemia. Cumulative 1,3-butadiene exposure was based on job exposure class, calendar time and length of time in job and was qualitative rather than quantitative as in the SBR study of Delzell *et al.* (2001). There was no suggestion of increasing risk with increasing 1,3-butadiene exposure. Because the exposure estimates were qualitative, it is not possible to determine the reasons for apparent absence of risk associated with 1,3-butadiene exposure in the monomer compared to the SBR study. It has been suggested that the lack of risk among monomer workers could be due to the absence of concomitant styrene and DMDTC exposures, or that 1,3-butadiene exposures were lower than the apparent threshold observed in the SBR study. The absence of risk among monomer workers is consistent with the lack of genotoxic effects among a small group of monomer workers from Prague (Albertini *et al.*, 2003). Biomarkers of exposure were related to 1,3-

butadiene exposure, but genotoxic effects were not related to 1,3-butadiene. Albertini *et al*. (2003) suggested that the lack of a genotoxic effect was not supportive of a cancer classification.

Conclusion

1,3-Butadiene is an animal carcinogen that demonstrates species differences in potency. 1,3-Butadiene is a potent, multi-site carcinogen in the mouse. Inhalation exposure to concentrations of 6.25 ppm produced lung tumors in B6C3F1 mice. Exposure to higher concentrations produced tumors at multiple sites. 1,3-Butadiene is a less potent carcinogen in rats. Although treatment related tumors were observed in the rat study, the potency and total tumor incidence was markedly different when compared to the mouse bioassays. The differences observed are likely due to the difference in 1,3-butadiene metabolism described in section 4.1.1.

Carcinogenic effects of 1,3-butadiene are more difficult to discern for humans. Epidemiology studies of workers exposed to 1,3-butadiene in the monomer industry demonstrated no increase in carcinogenic risk. In the synthetic rubber industry workers exposed to 1,3-butadiene demonstrated an increased risk of leukemia associated with long term exposure to high levels of 1,3-butadiene. The association was stronger when co-exposures to styrene and DMDTC were also considered. The difference in leukemia risk between these two groups could be related to differences in exposure to 1,3-butadiene, or the need for co-exposure to other agents in addition to 1,3-butadiene (styrene, DMDTC) for the expression of leukemia.

4.1.7 Toxicity for Reproduction

Several studies evaluated the reproductive and developmental toxicity of streams in the Crude Butadiene C4 Category (Tables 10 and 11). The streams evaluated ranged in 1,3-butadiene content from 10 to 100%. The majority of studies were conducted under standard protocols in compliance with GLP (good laboratory practices).

Table 10. Summary of Reproductive Toxicity Data

CAS RN and Stream Name (% 1,3-Butadiene)	Test Organism	OECD Test Guideline	NOAEL (mg/m^3)
68476-52-8 C4 Crude Butadiene (10)	Crl:CD Rat	422	>20,000 (Systemic) >20,000 (Reproductive)
106-99-0 1,3-Butadiene (>99)	Crl:CD Rat	421	>663 (Systemic) >13,260 (Reproductive)

Table 11. Summary of Developmental Toxicity Data

CAS RN and Stream Name (% 1,3-Butadiene)	Test Organism	OECD Test Guideline	NOAEL (mg/m^3)
68476-52-8 C4 Crude Butadiene (10)	Crl:CD Rat	422	>20,000 (Developmental) >20,000 (Maternal)
106-99-0 1,3-Butadiene (>99)	Crl:CD Rat	421	>13,260 (Developmental) >663 (Maternal)
106-99-0 1,3-Butadiene (>99)	CD Rat	414	>2,210 (Developmental) >442 (Maternal)
106-99-0 1,3-Butadiene (>99)	CD-1 Swiss Mice	414	>88.4 (Developmental) >88.4 (Maternal)

Effects on Fertility

Studies in Animals

Reproductive toxicity of C4 crude butadiene (CAS # 68476-52-8: 10% 1,3-butadiene; 4% isobutane; 4% n-butane; 29% trans-2-butene; 29% 1-butene; 11% isobutylene; and 12% cis-2-butene) was evaluated in an OECD 422 Repeat Dose Reproductive/Developmental Toxicity Screen (Carney *et al.*, 2001). Groups of 12 adult male and female Crl:CD Sprague-Dawley rats were exposed via inhalation to crude butadiene at concentrations of 0; 2,000; 10,000; or 20,000 mg/m^3, 6 hr/day, 7 days per week two weeks prior to breeding, during breeding, continuing to gestation day 19. Male rats were exposed for 36 to 37 days. No differences were observed in parental body weights, body weight gains or feed consumption between the groups. No treatment related effects were observed on mating, conception, fertility, or time to mating. Evaluations of gonadal function revealed no difference between treated and control groups. The NOAEL for reproductive toxicity was determined to be 20,000 mg/m^3.

Reproductive toxicity of 1,3-butadiene was evaluated in an OECD 421 inhalation reproduction and developmental toxicity screening test (WIL Research Laboratories, 2003). Adult male and female Crl:CD rats were exposed to concentrations of 0; 663; 3,313; or 13,260 mg/m^3 1,3-butadiene two week prior to breeding, during mating, gestation and lactation for a total of 83 to 84 consecutive days for F0 males, 60 to 70 total days for F0 females and 7 consecutive days for 2 groups of F1 offspring (one male and one female per litter on post natal days 21 to 27 or 28 to 34). In F0 and F1 animals a reduction in body weight was observed at 3,313 and 13,260 mg/m^3. Clinical signs of toxicity, chromodacryorrhea, chromorhinorrhea, and salivation in F0 animals as well as dried red material in the perioral and perinasal regions in the F1 pups were observed at 13,260 mg/m^3. No effect at any dose level was observed in any reproductive parameter examined including gonadal function, mating behavior, conception, gestation, parturition, and lactation. The systemic NOAEL for this study was 663 mg/m^3. The reproductive NOAEL was >13,260 mg/m^3.

The effect of 1,3-butadiene exposure on fertility in male mice was examined in a rodent dominant lethal test and sperm-head morphology assay (Morrissey, 1990). Male mice were exposed to 0; 442; 2,210; or 11,040 mg/m^3 1,3-butadiene via inhalation for 5 days, 6 hr/day. In the dominant lethal assay, CD-1 male mice were then mated to two unexposed female mice/week for eight consecutive weeks. In the two low dose groups slight differences were observed in ratio of dead to total implants, percentage of females with ≥2 dead implants and number of dead implants per pregnancy (also observed in the high dose group during week 1). No differences were observed in number of

pregnant females, implantations per litter, number of live fetuses, dead implantations/total implantations, or number of resorptions during weeks 1 and 2. No differences were observed for any endpoint during weeks 3 to 8. It was concluded, despite the lack of dose response, that 1,3-butadiene had an effect on mature germ cells. To assess sperm morphology, B6C3F1 mice were used and maintained for five weeks post exposure (Morrissey, 1990). At the end of the post exposure period, the reproductive tract was evaluated for gross lesions and sperm were obtained from the right cauda epididymus. A dose dependent increase in percentage of abnormal sperm was observed, becoming significantly different from control at the two highest exposure concentrations.

Developmental Toxicity

As part of an OECD 422 Repeat Dose Reproductive/Developmental Toxicity Screen (Carney *et al.*, 2001), no developmental toxicity was observed in Crl:CD Sprague-Dawley rats following exposure to C4 crude butadiene (CAS # 68476-52-8: 10% 1,3-butadiene; 4% isobutane; 4% n-butane; 29% trans-2-butene; 29% 1-butene; 11% isobutylene; and 12% cis-2-butene). Groups of 12 adult male and female rats were exposed via inhalation to crude butadiene at concentrations of 2, 10, or 20 mg/L (2,000; 10,000; or 20,000 mg/m^3), 6 hr/day, 7 days per week, 2 weeks prior to breeding, during breeding, and continuing to gestation day 19. No treatment related effects were observed in paternal body weights, body weight gains or feed consumption during the study. No difference was observed in number of viable litters, gestation length, litter size, pre implantation loss, pup body weight, or pup sex ratio. An increase was observed in post implantation loss in the low exposure group. This observation was considered spurious, given the lack of dose response. A single pup in the high dose group exhibited a hernia. This finding was considered spurious due to its low incidence. The NOAEL for this study was 20,000 mg/m^3.

A guideline OECD 414 developmental toxicity study was conducted in pregnant CD rats exposed to 0; 40; 200; or 1,000 ppm 1,3-butadiene on gestation days 6 to 15, 6 hr/day (Morrissey, 1990). Dams were sacrificed on gestation day 20. Decreased weight gain was observed in dams at 2,210 mg/m^3. There were no significant differences among the groups for number of live fetuses per litter, percent resorptions, malformations per litter, placental or fetal body weights or sex ratio. There was no evidence of developmental toxicity in any of the treated groups. The maternal NOAEL for this study was 442 mg/m^3 and the fetal NOAEL was 2,210 mg/m^3.

Developmental toxicity was evaluated in Crl:CD rats exposed to 0; 663; 3,313; or 13,260 mg/m^3 (0; 301; 1,507; or 6,006 ppm, respectively) 1,3-butadiene during the conduct of an OECD 421 inhalation reproduction and developmental toxicity screening test (WIL Research Laboratories, 2003). Adult male and female Crl:CD rats were exposed to 1,3-butadiene two week prior to breeding, during mating, gestation and lactation for a total of 83 to 84 consecutive days for F0 males, 60 to 70 total days for F0 females and 7 consecutive days for two groups of F1 offspring (one male and one female per litter on post natal days 21 to 27 or 28 to 34). In F1 offspring, a reduction in weight gain was observed in the 3,313 and 13,260 mg/m^3 groups during later stages of the lactation period. No indications of fetal toxicity or teratogenicity were observed. The systemic NOAEL for F0 and F1 animals was 663 mg/m^3. The developmental NOAEL was 13,260 mg/m^3.

Pregnant female CD-1 mice were exposed via inhalation to 0; 88.4; 442; or 2,210 mg/m^3 (0; 40; 200; or 1,000 ppm, respectively) 1,3-butadiene on day 6 to 15 of gestation, 6 hr/day using the OECD 414 developmental toxicity guideline (Morrissey, 1990). On day 18 of gestation, dams were sacrificed and maternal and fetal evaluations were made. Decreased maternal body weight gain was observed at 442 and 2,210 mg/m^3. Male and female fetal weights were reduced in the high dose groups. Placental weights were reduced for male fetuses at 200 ppm and males and females at 2,210 mg/m^3. Fetal variations (supernumary ribs and reduced sternebrae ossification) were increased in the 442 and 2,210 mg/m^3 groups. The maternal and developmental NOAEL for this study was 88.4 mg/m^3.

Conclusion

Effects on fertility and developmental toxicity of C4 Crude Butadiene (high butadiene concentration) are adequately defined with the available data. A stream with 1,3-butadiene concentration of approximately 10% produced no reproductive or developmental toxicity in rats exposed to concentrations as high as 20,000 mg/m^3. No reproductive or developmental toxicity was observed in rats exposed to concentrations up to 13,260 mg/m^3 1,3-butadiene. No developmental toxicity was observed in rats exposed to 2,210 mg/m^3 1,3-butadiene in the presence of maternal toxicity. These two streams cover the range of C4 Crude Butadiene streams (10% to approximately 100% 1,3-butadiene). As observed with other endpoints, mice are more susceptible than rats to developmental and reproductive toxicity of 1,3-butadiene, most likely due to an increased metabolic capacity in mice to form reactive metabolites. This is evident by the observation of developmental toxicity in mice at 442 mg/m^3 1,3-butadiene exposure. There is some indication of male mediated toxicity in mice following 1,3-butadiene exposure; however, the effect appears to be weak. As humans metabolize 1,3-butadiene in a manner more consistent with rats than mice, reproductive and developmental toxicity data developed in rats is more appropriate to use in assessing human risk.

The ability of 1,3-butadiene to cause ovarian atrophy is dependent on the production of the diepoxide metabolite and this differs between species (U.S. EPA, 2002). The mouse is the most sensitive species in terms of ovarian atrophy induction following 1,3-butadiene exposure while the rat is resistant to this effect. The observed species differences correlate with the production of the diepoxide metabolite of 1,3-butadiene, with the mouse producing higher levels of this toxic intermediate. Direct administration of the diepoxide metabolite of 1,3-butadiene can affect the rat ovary, albeit at higher dose levels than required for inducing similar effects in mice. Therefore, the mouse ovary is more sensitive to the toxic effects of both 1,3-butadiene and the diepoxide metabolite (U.S. EPA, 2002). Species differences in metabolism are explained in Section 4.1.1.

4.2 Assessment Summary for Human Health

Crude Butadiene C4 streams have a low order of acute toxicity. The components of Crude Butadiene C4 streams are gaseous at normal temperature and pressure; thus, ingestion or dermal absorption of this material is unlikely. Minimal effects were observed at concentrations of 5,300 mg/m^3.

Liquid Crude Butadiene C4 (test material was cooled in a dry ice bath) did not produce dermal or ocular irritation in rabbits. Exposure to liquid Crude Butadiene C4 is unlikely, as the components of the streams in this category are gases at normal temperature and pressure.

A species difference in repeated dose toxicity of Crude Butadiene C4 was apparent between rats and mice. Minimal effects were reported in rat repeated dose toxicity tests exposed to several Crude Butadiene C4 streams (1,3-butadiene content ranging from 10 to 99.2%). The no observable adverse effect levels were the highest concentrations tested or 17,679; 20,000; or 25,100 mg/m^3 (8,000; 9,060; or 11,365 ppm, respectively) following 90, 36, or 9 days or exposure, respectively. In contrast, mortality was observed in mice exposed to 2,761 mg/m^3 1,3-butadiene (99.2%) for 90 days. Well-documented species differences in 1,3-butadiene metabolism are the likely reason for the noted differences in repeat dose toxicity. Mice produce greater amounts of toxic metabolites following 1,3-butadiene exposure than rats. The existing metabolism data suggest that metabolism in humans appears to be more like metabolism in rats than in mice.

Test data demonstrate that Crude Butadiene C4 can produce genotoxicity. *In vitro*, Crude Butadiene C4 demonstrated little activity in reverse mutation assays conducted in *Salmonella typhimurium* either in the presence or absence of metabolic activation. In addition, Crude Butadiene C4 did not increase the number of transformed foci in C3H/10T1/2 clone 8 mouse embryo fibroblast cells. In the mouse lymphoma assay, evidence of mutagenic activity in mouse lymphoma L5178Y cells in

culture was observed in the absence of metabolic activation, but not in the presence of metabolic activation. *In vivo*, several Crude Butadiene C4 streams, containing 10 to 45% 1,3-butadiene, induced micronuclei formation in rats and mice following inhalation exposure.

Cancer data exist for 1,3-butadiene and these data are used as a surrogate for the Crude Butadiene C4 Category. Species differences exist in the carcinogenic response to 1,3-butadiene exposure. Similar to repeat dose data, mice are more sensitive than rats. Tumors are observed at lower exposure concentrations and at greater incidence than rats. In humans, an association between leukemia incidence and 1,3-butadiene exposure was observed in synthetic rubber workers exposed to 1,3-butadiene. The association was stronger when co-exposures to styrene and DMDTC were considered. No increase in leukemia incidence was observed in butadiene monomer workers.

No reproductive or developmental toxicity was observed in rats exposed to Crude Butadiene C4 during the conduct of an OECD 422 repeat dose reproductive/developmental toxicity screen. Exposures to concentrations of 20,000 mg/m^3 were without effect. Further, in a prenatal developmental toxicity study, inhalation exposure of pregnant rats to 1,3-butadiene on days 5 to 16 (inclusive) of gestation elicited no developmental toxicity at any tested concentration up to 2,210 mg/m^3. Maternal toxicity was observed at levels of 442 mg/m^3. Similar to observations of species differences in repeat dose toxicity, mice were more sensitive than rats in developmental and reproductive toxicity following exposure to 1,3-butadiene. This increased sensitivity was apparent in effects on male germ cells observed in a dominant lethal study and an assessment of sperm morphology in male mice and fetal effects observed in a prenatal developmental toxicity study. Chronic exposure to 1,3-butadiene increased the incidence of ovarian atrophy in mice, most likely related to the formation of butadiene diepoxide.

5 HAZARDS TO THE ENVIRONMENT

5.1 Aquatic Toxicity

The aquatic toxicity of streams in this category is expected to fall within a relatively narrow range regardless of their composition. This is expected because the constituent chemicals of these streams are neutral organic hydrocarbons whose toxic mode of action is non-polar narcosis (Ramos *et al.*, 1998). The toxic mechanism of short-term toxicity for these chemicals is disruption of biological membrane function (Van Wezel, 1995), and the differences between toxicities (i.e., LC/LL_{50}, EC/EL_{50}) can be explained by the differences between the target tissue-partitioning behavior of individual constituent chemicals (Verbruggen *et al.*, 2000).

The existing fish toxicity database for hydrophobic, neutral organic chemicals, which comprise the streams in this category, supports a critical body residue (CBR) for these chemicals between approximately 2-8 mmol/kg fish (wet weight) (McCarty *et al.*, 1991; McCarty and Mackay, 1993). The CBR is the internal concentration of a toxicant that causes mortality. When normalized to lipid content for most organisms, the CBR is approximately 50 µmol/g of lipid (Di Toro, 2000). Therefore, only hydrocarbon streams with components of sufficient water solubility, such that their molar sum in solution is high enough to produce a total partitioning to the organism of approximately 50 µmol of hydrocarbon per gram of lipid will demonstrate lethality.

Measured data are not available for the aquatic toxicity endpoints. However, structure-activity relationship (SAR) data developed with the ECOSAR model (Cash and Nabholz, 1999) were used to assess the aquatic toxicity for three trophic levels [the ECOSAR model used was from EPIWIN (1999)]. The ECOSAR model is a reliable and valid SAR model to apply to constituent chemicals from this category because it is based on a related chemical dataset that calculates the toxicity of neutral organic hydrocarbons whose toxic mode of action is non-polar narcosis. The calculated

aquatic toxicity values were determined using measured log P_{ow} values (ECOSAR requires selected physicochemical data and chemical structure to calculate effect concentrations).

Calculated aquatic toxicity values for chemicals representative of category members fall within a relatively narrow range. The effect range is a function of the range of log P_{ow} values identified for the chemicals. Streams in this category are expected to demonstrate 96-hour LC_{50} fish toxicity values in the range of 6.28 to 40.98 mg/L, 48-hour LC_{50} invertebrate toxicity values in the range of 7.15 to 43.88 mg/L, and 96-hour EC_{50} alga toxicity values in the range of 4.71 to 27.42 mg/L (Table 12).

Table 12. Summary of Aquatic Toxicity Data for Chemical Constituents in the Crude Butadiene C4 Category

Chemical Constituent (Log P_{ow}*)	Fish Toxicity 96-hour LC_{50} (mg/L)	Invertebrate Toxicity 48-hour EC_{50} (mg/L)	Alga Toxicity 96-hour EC_{50} (mg/L)
Isobutane (2.76)	8.32	9.39	6.13
n-Butane (2.89)	6.28	7.15	4.71
Isobutylene (2.34)	19.93	21.86	13.94
cis-Butene-2 (2.31)	21.26	23.28	14.81
trans-Butene-2 (2.33)	20.36	22.32	14.22
Butene-1 (2.40)	17.50	19.28	12.33
1,3-Butadiene (1.99)	40.98	43.88	27.42

* The log P_{ow} values used in the ECOSAR model are from the EPIWIN experimental database.

5.2 Assessment Summary for the Environment

Results of distribution modeling show that streams in the Crude Butadiene C4 Category will partition primarily to the air compartment, with a negligible amount partitioning to water. Although constituents have a moderate degree of water solubility, wet deposition of category constituents is not likely to play a significant role in their atmospheric fate because they rapidly photodegrade. Volatilization to the air will contribute to the rapid loss of category constituents from aqueous and terrestrial habitats. In the air, these constituents have the potential to rapidly degrade through indirect photolytic processes mediated primarily by hydroxyl radicals with calculated degradation half-lives ranging from 1.9 to 52.6 hours, depending on hydroxyl radical concentration. Aqueous photolysis and hydrolysis will not contribute to the transformation of category constituents in aquatic environments because they are either poorly or not susceptible to these reactions.

Although the biodegradability of streams in this category has not been evaluated with standard testing procedures because of their high volatility, studies have demonstrated that several category constituents can be degraded by bacteria isolated from soil and surface water samples. The results from these studies suggest that streams from this category are subject to microbial degradation. However, biodegradation is unlikely to contribute to the overall degradation of these streams because they tend to partition to the air compartment due to high volatility at ambient temperatures, and thus are less likely to be available to degrading microorganisms.

Due to the fact that streams in this category are gaseous at ambient temperature and pressure and expected to partition predominantly to the atmosphere, no aquatic toxicity testing was conducted. However, the ECOSAR model was used to predict aquatic toxicity using the equation for neutral organics, a reliable estimation method for this class of chemicals. Calculated acute toxicity values of selected category constituents for fish (96-hr) and invertebrates (48-hr) range from 6.28 to 40.98

mg/L and from 7.15 to 43.88 mg/L, respectively. For algae, the calculated 96-hr EC_{50} ranges from 4.71 to 27.42 mg/L.

6 DATA SUMMARY

Physico-chemical, environmental fate and effects, and human health data that characterize the two streams in the Crude Butadiene C4 Category are summarized in Tables 13 and 14. CAS RNs are associated with streams as follows:

- **C4 Crude Butadiene Stream**
  - 68476-52-8
  - 68187-60-0
  - 68955-28-2
  - 64742-83-2
  - 68476-44-8
  - 68956-54-7
  - 68477-41-8
  - 25167-67-3
- **Butadiene Unit Heavy Ends Stream**
  - 69103-05-5
  - 68477-41-8
  - 68512-91-4

Table 13. Physico-Chemical and Environmental Data Used to Characterize Streams and CAS RNs in the Crude Butadiene C4 Category (ranges are based on data for the most representative chemical subset for category streams and CAS RNs)

Endpoint	Crude Butadiene C4 Category Streams and CAS RNs								
							Butadiene Unit Heavy Ends Stream		
	C4 Crude Butadiene Stream								
	68955-28-2	68476-44-8	25167-67-3	68187-60-0	68476-52-8	68956-54-7	68477-41-8	68512-91-4	69103-05-5
Melting Point*/ Range (°C)	-145.0 to -105.5 (m)								
Boiling Point*/ Range (°C)	-11.7 to 0.8 (m)								
Vapor Pressure*/ Range (hPa)	2.33 E3 to 3.08 E3 (m)								
Log P_{ow}*/ Range	1.99 to 2.89 (m)								
Water Solubility*/ Range (mg/L)	135.6 to 792.3 (m)								
Direct Photodegradation	Direct photolysis will not contribute to degradation								
Indirect (OH-) Photodegradation* (half-life, hrs) (c)	1.9 to 52.6 (a)								
Hydrolysis	Hydrolysis will not contribute to degradation								
Distribution*	>99.9% partitions to air <0.1% partitions to water								
Biodegradation	Potential to biodegrade								
96-hr Fish Acute Toxicity* (mg/L)	22.03 to 37.59 (c)								
48-hr Invert Acute Toxicity* (mg/L)	24.11 to 40.27 (c)								
96-hr Alga Toxicity* (mg/L)	15.35 to 25.27 (c)								

* Constituent chemicals used to define selected endpoints include: isobutane; n-butane; isobutylene; cis-butene-2; trans-butene-2; butene-1; 1,3-butadiene
(m) Measured values (c) Calculated values (a) Atmospheric half-life values are based on a 12-hr day.

Table 14. Human Health Data Summary Used to Characterize Streams and CAS RNs in the Crude Butadiene C4 Category

Endpoint	Human Health Data Based on 1,3-Butadiene Content (wt%) for Crude Butadiene C4 Category Streams (CAS RNs)									
	10%	20	30	40	50	60	70	80	90	100
	C4 Crude Butadiene Stream (64742-83-2, 68955-28-2, 68476-44-8, 25167-67-3, 68187-60-0, 68476-52-8, 68956-54-7, 68477-41-8)									
	Butadiene Unit Heavy Ends Stream (68477-41-8, 68512-91-4, 69103-05-5)									
Acute Toxicity (rat)	LC50 >5,300 mg/m^3									LC50 =285,000 mg/m^3
Irritation						Non Irritating (eyes / skin)				
Repeat Dose Toxicity (rat)	NOAEL >20,000 mg/m^3			NOAEL >25,100 mg/m^3						NOAEL >17,679 mg/m^3
Mutagenicity Ames Assay						Negative				Weakly Positive
Mutagenicity Mouse Micronucleus	Positive			Positive						Positive
Reproductive Toxicity (rat)	NOAEL >20,000 mg/m^3									NOAEL >13,260 mg/m^3
Developmental Toxicity (rat)	NOAEL (M&F) >20,000 mg/m^3									NOAEL (M) >663 mg/m^3 NOAEL (F) >13,260 mg/m^3

M Male F Female

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APPENDIX I

ETHYLENE PROCESS DESCRIPTION

A. Ethylene Process

1. Steam Cracking

Steam cracking is the predominant process used to produce ethylene. Various hydrocarbon feedstocks are used in the production of ethylene by steam cracking, including ethane, propane, butane, and liquid petroleum fractions such as condensate, naphtha, and gas oils. The feedstocks are normally saturated hydrocarbons but may contain minor amounts of unsaturates. These feedstocks are charged to the coils of a cracking furnace. Heat is transferred through the metal walls of the coils to the feedstock from hot flue gas, which is generated by combustion of fuels in the furnace firebox. The outlet of the cracking coil is usually maintained at relatively low pressure in order to obtain good yields to the desired streams. Steam is also added to the coil and serves as a diluent to improve yields and to control coke formation. This step of the ethylene process is commonly referred to as "steam cracking" or simply "cracking" and the furnaces are frequently referred to as "crackers".

Subjecting the feedstocks to high temperatures in this manner results in the partial conversion of the feedstock to olefins. In the simplest example, feedstock ethane is partially converted to ethylene and hydrogen. Similarly, propane, butane, or the hydrocarbon compounds that are associated with the liquid feedstocks are also converted to ethylene. Other valuable hydrocarbon streams are also formed, including other olefins, diolefins, aromatics, paraffins, and lesser amounts of acetylenes. These other hydrocarbon streams include compounds with two or more carbon (C) atoms per molecule, i.e., C2, C3, C4, etc. Propane and propylene are examples of C3 hydrocarbons and benzene, hexene, and cyclohexane are a few examples of the C6 hydrocarbons.

2. Refinery Gas Separation

Ethylene and propylene are also produced by separation of these olefins streams, such as from the light ends product of a catalytic cracking process. This separation is similar to that used in steam crackers, and in some cases both refinery gas streams and steam cracking furnace effluents are combined and processed in a single finishing section. These refinery gas streams differ from cracked gas in that the refinery streams have a much narrower carbon number distribution, predominantly C2 and/or C3. Thus the finishing of these refinery gas streams yields primary ethylene and ethane, and/or propylene and propane.

B. Crude Butadiene C4 Streams from the Ethylene Process

The intermediate stream that exits the cracking furnaces (i.e., the furnace effluent) is forwarded to the finishing section of the ethylene plant. The furnace effluent is commonly referred to as "cracked gas" and consists of a mixture of hydrogen, methane, and various hydrocarbon compounds with two or more carbon atoms per molecule (C2+). The relative amount of each constituent in the cracked gas varies depending on what feedstocks are cracked and cracking process variables. Cracked gas may also contain relatively small concentrations of organic sulfur compounds that were present as impurities in the feedstock or were added to the feedstock to control coke formation. The cracked gas stream is cooled, compressed and then separated into the individual streams of the ethylene process. These streams can be sold commercially and/or put into further steps of the process to produce additional materials. In some ethylene processes, a liquid fuel oil stream is produced when the cracked gas is initially cooled. The ethylene process is a closed process and the streams are contained in pressure systems. (See Figure 4 for a pictorial representation of the ethylene manufacturing process.)

The final streams from the ethylene process include hydrogen, methane (frequently used as fuel), and the high purity chemicals, ethylene and propylene. Other streams from the ethylene process are

typically mixed streams that are isolated by distillation according to boiling point ranges. It is a subset of these mixed streams that make up streams in the Crude Butadiene C4 Category.

C. Crude Butadiene C4 Category Streams

1. C4 Crude Butadiene

The C4 Crude Butadiene stream (previously referred to as Butadiene Concentrate stream) is separated by distillation from the condensed portion of the cracked gas. Typically, C4 Crude Butadiene is a fairly narrow boiling range mixture consisting predominately of C4 hydrocarbons. C4 Crude Butadiene may also contain lesser amounts of C3 or lighter hydrocarbons and C5 and heavier hydrocarbons, because the separation technology is not perfect. The 1,3-butadiene content of these streams is typically 40 to 60%, but can range from approximately 10 to 82% (Table 2). C4 Crude Butadiene streams are sometimes produced in "on purpose" butadiene units using, for example, an oxydehydrogenation process.

2. Butadiene Unit Heavy Ends

Several different technologies are used to separate 1,3-butadiene from the C4 Crude Butadiene stream produced by the ethylene process. All of these technologies use a solvent to effect the separation.

In one technology, the C4 Crude Butadiene stream is fed to an extractive distillation (ED) column and a C4 mixture referred to as “raffinate” (i.e., C4 olefins and paraffins) is separated from the top of the distillate column. The bottom from the ED column consists of solvent rich in 1,3-butadiene and small amounts of other C4s. The rich solvent is fed to the solvent stripper where the 1,3-butadiene and other C4s are taken overhead (removed). The stripped, lean solvent is transferred from the bottom of the stripper back to the ED tower. The overhead of the stripper is condensed and fed to the rerun tower (or postfractionator) where high purity 1,3-butadiene is produced as the overhead. Bottoms of the rerun tower consist of the higher boiling constituents of C4 Crude Butadiene stream (e.g., 1,2-butadiene). The 1,3-butadiene content of streams in the Butadiene Unit Heavy Ends stream (previously referred to as High Butadiene Heavy Ends) covered by this test plan can range from 13 to 92% (Table 2).

3. Pyrolysis C3+ and Pyrolysis C4+

Butadiene concentrate sometimes consists of the entire C3+ or C4+ portion of the cracked gas stream (Pyrolysis C3+ and C4+ streams, previously referred to as Full Range Butadiene Concentrate stream). In this case, the carbon number distribution is between C3 and C12 or even higher. Normally the C4+ full-range 1,3-butadiene concentrate is split by distillation into two streams, a C4 Crude Butadiene stream, described above, and pyrolysis gasoline stream. The C3+ stream is separated into these two streams plus a C3 stream. The C3 stream (Propylene Streams Category) and pyrolysis gasoline (High Benzene Naphthas Category) are covered by separate categories sponsored by the Olefins Panel of the American Chemistry Council (Table 15). There are only two examples where these broad-range streams have been reported to have been isolated. In both cases, it was a result of a shutdown of process equipment and not the result of routine production conditions. The Pyrolysis C4+ stream was site limited and the Pyrolysis C3+ was not. The 1,3-butadiene content of Pyrolysis C3+ and Pyrolysis C4+ streams can range from 12 to 42% (Table 2). The Pyrolysis C3+ and Pyrolysis C4+ streams are discussed as a separate category.

4. 1,3-Butadiene

High purity 1,3-butadiene (99.5%+) is produced by separation from C4 crude butadiene produced by the ethylene process. This separation is accomplished by using a solvent process, either extraction or more typically extractive distillation. “On purpose” units also produce a small percentage of the commercially available 1,3-butadiene by dehydrogenation and subsequent separation.

Figure 5. Crude Butadiene C4 Process Streams Flow Diagram from the Ethylene Manufacturing Process Unit

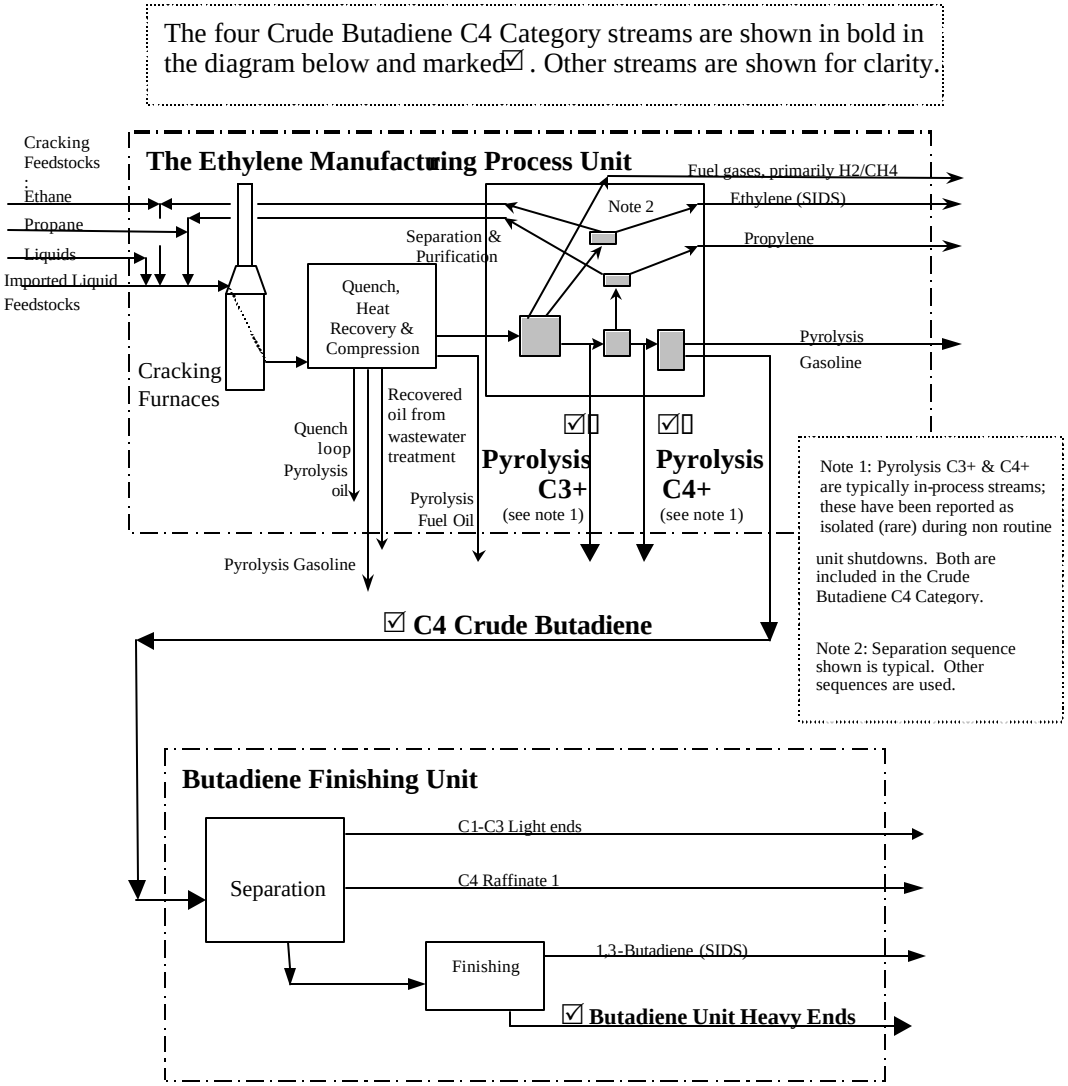


Table 15. HPV Program Categories Sponsored by the Olefins Panel of the American Chemistry Council

Category Number	Category Name
1	Crude Butadiene C4
2	Low 1,3-Butadiene C4
3	C5 Non-Cyclics
4	Propylene Streams
5	High Benzene Naphthas
6	Low Benzene Naphthas
7,8,9	Resin Oils & Cyclodiene Dimer Concentrates
10	Fuel Oils
11	Pyrolysis C3+ and Pyrolysis C4+

APPENDIX II

201-15232A

ROBUST SUMMARIES OF STUDIES USED TO CHARACTERIZE THE CRUDE BUTADIENE C4 CATEGORY

PHYSICO-CHEMICAL ROBUST SUMMARIES

Melting Point

Test Substance*:	Other TS
Method/Guideline:	Calculated values using MPBPWIN version 1.40, a subroutine of the computer program EPIWIN version 3.04
Year (guideline):	1999
Type (test type):	Not applicable
GLP:	Not applicable
Year (study performed):	Not applicable
Test Conditions: (FT - TC) • **Note: Concentration prep., vessel type, replication, test conditions.**	Melting Point estimations performed by MPBPWIN are based on the average result of the calculation methods of K. Joback and Gold and Ogle. Joback's Method is described in Joback, K.G. 1982. A Unified Approach to Physical Property Estimation Using Multivariate Statistical Techniques. In The Properties of Gases and Liquids. Fourth Edition. 1987. R.C. Reid, J.M. Prausnitz and B.E. Poling, Eds. The Gold and Ogle Method simply uses the formula Tm = 0.5839Tb, where Tm is the melting point in Kelvin and Tb is the boiling point in Kelvin.
Results: (FT - RS) **Units/Value:** • **Note: Deviations from protocol or guideline, analytical method.**	Chemical / Calculated MP (°C) / Measured* MP (°C) Isobutane: -132.55 / -138.3 n-butane: -120.28 / -138.2 isobutylene: -130.88 / -140.4 cis-butene-2: -120.41 / -105.5 trans-butene-2: -120.41 / -105.5 butene-1: -121.74 / -145.0 1,3-butadiene: -123.21 / -108.9 * Experimental values are supplied by the MPBPWIN program database (EXP_MBVP.DB) which contains more than 11,000 organic compounds with reliably measured

	values which are taken from SRC's PHYSPROP Database. Commercial products in this category can have a carbon number distribution predominantly between C3 and C5. These products can contain significant levels of 1,3-butadiene and similar low molecular weight olefins, which is why they are considered a category for purposes of the High Production Volume Chemical Program, and designated Crude Butadiene C4. The seven chemicals selected to represent the melting range of this category are C4 hydrocarbons that are common across the 10 CAS numbers. Crude butadiene category products arise from production processes associated with ethylene manufacturing. More information on the Crude Butadiene C4 Category can be found in the American Chemistry Council, Olefins Panel test plan for this category (1). 1. Olefins Panel, HPV Implementation Task Group. 2001. High Production Volume (HPV) Chemical Challenge Program Test Plan For The Crude Butadiene C4 Category. American Chemistry Council, Olefins Panel, HPV Implementation Task Group. VA, USA.
Test Substance: (FT - TS)	25167-67-3 Butenes 68477-41-8 Distillate (Petroleum), Extractive C3-5 68955-28-2 Gases, (Petroleum) Light Steam Cracked, Butadiene Concentrate 68476-44-8 Hydrocarbons, >C3 68512-91-4 Hydrocarbons C3 – C4 Rich Petroleum Distillates 68187-60-0 Hydrocarbons, C4, Ethane-Propane Cracked 68476-52-8 Hydrocarbons, C4, Ethylene Manufactured By-Product 68956-54-7 Hydrocarbons C4, Unsaturated 69103-05-5 Hydrocarbons, C4-7, Butadiene Manufactured By-Product 64742-83-2 Naphtha, (Petroleum), Light Steam-Cracked
Conclusion: (FT - CL)	Based on the calculated values, products in this category can have a melting range of -132.55 to -120.28 °C. Based on the measured values, products in this category can have a melting range of -145.0 to -105.5°C.
Reliability: (FT - RL)	(2) Reliable with restrictions The results include calculated values based on the chemical structure and experimental values available in the

	MPBPWIN program and represent a potential melting range for products with the 10 CAS numbers listed under Test Substance.
Reference: (FT - RE)	Meylan, M., SRC 1994-1999. WSKOWWIN is contained in the computer program EPIWIN. 1999. Estimation Program Interface for Windows, version 3.04. Syracuse Research Corporation, Syracuse, NY, USA.
Other (source): (FT - SO)	American Chemistry Council, Olefins Panel

* Other TS is an option in the "test substance" pick list within the IUCLID data entry field for "melting point". Selecting this option refers the reader to information in the "freetext" field for "test substance".

FT - Freetext

IUCLID fields include:

RL - Reliability
TC - Test Conditions
RE - Reference
RS - Results
TS - Test Substance
SO - Source
CL - Conclusion

Boiling Point

Test Substance*:	Other TS
Method/Guideline:	Calculated values using MPBPWIN version 1.40, a subroutine of the computer program EPIWIN version 3.04
Year (guideline):	1999
Type (test type):	Not applicable
GLP:	Not applicable
Year (study performed):	Not applicable
Estimation Pressure:	760 mm Hg
Test Conditions: (FT - TC) • **Note: Concentration prep., vessel type, replication, test conditions.**	Boiling Point estimations performed by MPBPWIN are based on the calculation method of S. Stein and R. Brown in "Estimation of Normal Boiling Points from Group Contributions". 1994. J. Chem. Inf. Comput. Sci. **34**: 581-587.
Results: (FT - RS) **Units/Value:** • **Note: Deviations from protocol or guideline, analytical method.**	<u>Chemical</u> — <u>Calculated BP (°C)</u> — <u>Measured* BP (°C)</u> Isobutane — 3.21 — -11.7 n-butane — 19.58 — -0.5 isobutylene — 10.18 — -6.9 cis-butene-2 — 27.82 — 0.8 trans-butene-2 — 27.82 — 0.8 butene-1 — 17.57 — -1.3 1,3-butadiene — 15.55 — -4.4 * Experimental values are supplied by the MPBPWIN program database (EXP_MBVP.DB) which contains more than 11,000 organic compounds with reliably measured values which are taken from SRC's PHYSPROP Database. Commercial products in this category can have a carbon number distribution predominantly between C3 and C5. These products can contain significant levels of 1,3-butadiene and similar low molecular weight olefins, which is why they are considered a category for purposes of the High Production Volume Chemical Program, and designated <u>Crude Butadiene C4.</u> The seven chemicals selected to represent the boiling range of this category are C4 hydrocarbons that are common across the 10 CAS numbers. Crude butadiene category

	products arise from production processes associated with ethylene manufacturing. More information on the Crude Butadiene C4 Category can be found in the American Chemistry Council, Olefins Panel test plan for this category (1). 1. Olefins Panel, HPV Implementation Task Group. 2001. High Production Volume (HPV) Chemical Challenge Program Test Plan For The Crude Butadiene C4 Category. American Chemistry Council, Olefins Panel, HPV Implementation Task Group. VA, USA.
Test Substance: (FT - TS)	25167-67-3 Butenes 68477-41-8 Distillate (Petroleum), Extractive C3-5 68955-28-2 Gases, (Petroleum) Light Steam Cracked, Butadiene Concentrate 68476-44-8 Hydrocarbons, >C3 68512-91-4 Hydrocarbons C3 – C4 Rich Petroleum Distillates 68187-60-0 Hydrocarbons, C4, Ethane-Propane Cracked 68476-52-8 Hydrocarbons, C4, Ethylene Manufactured By-Product 68956-54-7 Hydrocarbons C4, Unsaturated 69103-05-5 Hydrocarbons, C4-7, Butadiene Manufactured By-Product 64742-83-2 Naphtha, (Petroleum), Light Steam-Cracked
Conclusion: (FT - CL)	Based on the calculated values, products in this category can have a boiling range of 3.21 to 27.82 °C. Based on the measured values, products in this category can have a boiling range of -11.7 to 0.8°C.
Reliability: (FT - RL)	(2) Reliable with restrictions The results include calculated values based on the chemical structure and experimental values available in the MPBPWIN program and represent a potential boiling point range for products with the 10 CAS numbers listed under Test Substance.
Reference: (FT - RE)	Meylan, M., SRC 1994-1999. WSKOWWIN is contained in the computer program EPIWIN. 1999. Estimation Program Interface for Windows, version 3.04. Syracuse Research Corporation, Syracuse, NY, USA.
Other (source): (FT - SO)	American Chemistry Council, Olefins Panel

* Other TS is an option in the "test substance" pick list within the IUCLID data entry field for "boiling point". Selecting this option refers the reader to information in the "freetext" field for "test substance".

FT - Freetext
IUCLID fields include:
- RL - Reliability
- TC - Test Conditions
- RE - Reference
- RS - Results
- TS - Test Substance
- SO - Source
- CL - Conclusion

Vapor Pressure

Test Substance*:	Other TS
Method/Guideline:	Calculated values using MPBPWIN version 1.40, a subroutine of the computer program EPIWIN version 3.04
Year (guideline):	1999
Type (test type):	Not applicable
GLP:	Not applicable
Year (study performed):	Not applicable
Estimation Temperature:	25°C
Test Conditions: (FT - TC) • **Note: Concentration prep., vessel type, replication, test conditions.**	Vapor Pressure estimations performed by MPBPWIN are based on the average result of the calculation methods of Antoine and Grain. Both methods use boiling point for the calculation. The Antoine Method is described in the Handbook of Chemical Property Estimation. Chapter 14. W.J. Lyman, W.F. Reehl and D.H. Rosenblatt, Eds. Washington, D.C.: American Chemical Society. 1990. A modified Grain Method is described on page 31 of Neely and Blau's Environmental Exposure from Chemicals, Volume 1, CRC Press. 1985.
Results: (FT - RS) **Units/Value:** • **Note: Deviations from protocol or guideline, analytical method.**	Chemical — Calculated VP (hPa) — Measured* VP (hPa) Isobutane — 3.45 E^3 — 3.08 E^3 n-butane — 2.41 E^3 — 2.43 E^3 isobutylene — 2.97 E^3 — 3.08 E^3 cis-butene-2 — 2.31 E^3 — 2.33 E^3 trans-butene-2 — 2.31 E^3 — 2.33 E^3 butene-1 — 2.48 E^3 — 3.00 E^3 1,3-butadiene — 2.73 E^3 — 2.81 E^3 * Experimental values are supplied by the MPBPWIN program database (EXP_MBVP.DB) which contains more than 11,000 organic compounds with reliably measured values which are taken from SRC's PHYSPROP Database. Commercial products in this category can have a carbon number distribution predominantly between C3 and C5. These products can contain significant levels of 1,3-butadiene and similar low molecular weight olefins, which is

	why they are considered a category for purposes of the High Production Volume Chemical Program, and designated Crude Butadiene C4. The seven chemicals selected to represent the vapor pressure range of this category are C4 hydrocarbons that are common across the 10 CAS numbers. Crude butadiene category products arise from production processes associated with ethylene manufacturing. More information on the Crude Butadiene C4 Category can be found in the American Chemistry Council, Olefins Panel test plan for this category (1). 1. Olefins Panel, HPV Implementation Task Group. 2001. High Production Volume (HPV) Chemical Challenge Program Test Plan For The Crude Butadiene C4 Category. American Chemistry Council, Olefins Panel, HPV Implementation Task Group. VA, USA.
Test Substance: (FT - TS)	25167-67-3 Butenes 68477-41-8 Distillate (Petroleum), Extractive C3-5 68955-28-2 Gases, (Petroleum) Light Steam Cracked, Butadiene Concentrate 68476-44-8 Hydrocarbons, >C3 68512-91-4 Hydrocarbons C3 – C4 Rich Petroleum Distillates 68187-60-0 Hydrocarbons, C4, Ethane-Propane Cracked 68476-52-8 Hydrocarbons, C4, Ethylene Manufactured By-Product 68956-54-7 Hydrocarbons C4, Unsaturated 69103-05-5 Hydrocarbons, C4-7, Butadiene Manufactured By-Product 64742-83-2 Naphtha, (Petroleum), Light Steam-Cracked
Conclusion: (FT - CL)	Based on the calculated values, products in this category can have a vapor pressure range of 2.31 E^3 to 3.45 E^3 hPa. Based on the measured values, products in this category can have a vapor pressure range of 2. 33 E^3 to 3.08 E^3 hPa.
Reliability: (FT - RL)	(2) Reliable with restrictions The results include calculated values based on the chemical structure and experimental values available in the MPBPWIN program and represent a potential vapor pressure range for products with the 10 CAS numbers listed under Test Substance.
Reference: (FT - RE)	Meylan, M., SRC 1994-1999. MPBPWIN is contained in the computer program EPIWIN. 1999. Estimation Program

	Interface for Windows, version 3.04. Syracuse Research Corporation, Syracuse, NY, USA.
Other (source): (FT - SO)	American Chemistry Council, Olefins Panel

* Other TS is an option in the "test substance" pick list within the IUCLID data entry field for "vapor pressure". Selecting this option refers the reader to information in the "freetext" field for "test substance".

FT - Freetext

IUCLID fields include:

RL - Reliability
TC - Test Conditions
RE - Reference
RS - Results
TS - Test Substance
SO - Source
CL - Conclusion

Partition Coefficient

Test Substance*:	Other TS
Method/Guideline:	Calculated values using KOWWIN version 1.65, a subroutine of the computer program EPIWIN version 3.04
Year (guideline):	1999
Type (test type):	Not applicable
GLP:	Not applicable
Year (study performed):	Not applicable
Estimation Temperature:	25°C
Test Conditions: (FT - TC) • **Note: Concentration prep., vessel type, replication, test conditions.**	Octanol / Water Partition Coefficient estimations performed by KOWWIN are based on an atom/fragment contribution method of W. Meylan and P. Howard in "Atom/fragment contribution method for estimating octanol-water partition coefficients". 1995. *J. Pharm. Sci*. **84**:83-92.
Results: (FT - RS) **Units/Value:** • **Note: Deviations from protocol or guideline, analytical method.**	Chemical / Calculated log K_{ow} / Measured* log K_{ow} Isobutane 2.23 2.76 n-butane 2.31 2.89 isobutylene 2.23 2.34 cis-butene-2 2.09 2.31 trans-butene-2 2.09 2.33 butene-1 2.17 2.40 1,3-butadiene 2.03 1.99 * Experimental K_{ow} values supplied by the KOWWIN program database (EXPKOW.DB) which contains more than 13,000 organic compounds with reliably measured values. Commercial products in this category can have a carbon number distribution predominantly between C3 and C5. These products can contain significant levels of 1,3-butadiene and similar low molecular weight olefins, which is why they are considered a category for purposes of the High Production Volume Chemical Program, and designated Crude Butadiene C4. The seven chemicals selected to represent the partition coefficient range of this category are C4 hydrocarbons that are common across the 10 CAS numbers. Crude butadiene

	category products arise from production processes associated with ethylene manufacturing. More information on the Crude Butadiene C4 Category can be found in the American Chemistry Council, Olefins Panel test plan for this category (1). 1. Olefins Panel, HPV Implementation Task Group. 2001. High Production Volume (HPV) Chemical Challenge Program Test Plan For The Crude Butadiene C4 Category. American Chemistry Council, Olefins Panel, HPV Implementation Task Group. VA, USA.
Test Substance: (FT - TS)	25167-67-3 Butenes 68477-41-8 Distillate (Petroleum), Extractive C3-5 68955-28-2 Gases, (Petroleum) Light Steam Cracked, Butadiene Concentrate 68476-44-8 Hydrocarbons, >C3 68512-91-4 Hydrocarbons C3 – C4 Rich Petroleum Distillates 68187-60-0 Hydrocarbons, C4, Ethane-Propane Cracked 68476-52-8 Hydrocarbons, C4, Ethylene Manufactured By-Product 68956-54-7 Hydrocarbons C4, Unsaturated 69103-05-5 Hydrocarbons, C4-7, Butadiene Manufactured By-Product 64742-83-2 Naphtha, (Petroleum), Light Steam-Cracked
Conclusion: (FT - CL)	Based on the calculated K_{ow} values, products in this category can have a partition coefficient range of 2.03 to 2.31. Based on the measured K_{ow} values, products in this category can have a partition coefficient range of 1.99 to 2.89.
Reliability: (FT - RL)	(2) Reliable with restrictions The results include calculated values based on the chemical structure and experimental values available in the KOWWIN program and represent a potential partition coefficient range for products with the 10 CAS numbers listed under Test Substance.
Reference: (FT - RE)	Meylan, M., SRC 1994-1999. KOWWIN is contained in the computer program EPIWIN. 1999. Estimation Program Interface for Windows, version 3.04. Syracuse Research Corporation, Syracuse, NY, USA.
Other (source): (FT - SO)	American Chemistry Council, Olefins Panel

* Other TS is an option in the "test substance" pick list within the IUCLID data entry field for "partition coefficient". Selecting this option refers the reader to information in the "freetext" field for "test substance".

FT - Freetext
IUCLID fields include:
- RL - Reliability
- TC - Test Conditions
- RE - Reference
- RS - Results
- TS - Test Substance
- SO - Source
- CL - Conclusion

Water Solubility

Test Substance*:	Other TS
Method/Guideline:	Calculated values using WSKOWWIN version 1.36, a subroutine of the computer program EPIWIN version 3.04
Year (guideline):	1999
Type (test type):	Not applicable
GLP:	Not applicable
Year (study performed):	Not applicable
Estimation Temperature:	25°C
Test Conditions: (FT - TC) • **Note: Concentration prep., vessel type, replication, test conditions.**	Water Solubility estimations performed by WSKOWWIN are based on a Kow correlation method described by W. Meylan, P. Howard and R. Boethling in "Improved method for estimating water solubility from octanol/water partition coefficient". *Environ. Toxicol. Chem*. **15**:100-106. 1995.
Results: (FT - RS) **Units/Value:** • **Note: Deviations from protocol or guideline, analytical method.**	Chemical / Calculated WS (mg/L) / Measured* WS (mg/L) Isobutane 496.4 175.1 n-butane 424.1 135.6 isobutylene 495.6 399.2 cis-butene-2 652.7 423.5 trans-butene-2 652.7 407.1 butene-1 557.7 354.8 1,3-butadiene 732.4 792.3 * Experimental K_{ow} values supplied by the WSKOWWIN program database (EXPKOW.DB) which contains more than 13,000 organic compounds with reliably measured values. Commercial products in this category can have a carbon number distribution predominantly between C3 and C5. These products can contain significant levels of 1,3-butadiene and similar low molecular weight olefins, which is why they are considered a category for purposes of the High Production Volume Chemical Program, and designated Crude Butadiene C4. The seven chemicals selected to represent the water solubility range of this category are C4 hydrocarbons that are common across the 10 CAS numbers. Crude butadiene

	category products arise from production processes associated with ethylene manufacturing. More information on the Crude Butadiene C4 Category can be found in the American Chemistry Council, Olefins Panel test plan for this category (1). 1. Olefins Panel, HPV Implementation Task Group. 2001. High Production Volume (HPV) Chemical Challenge Program Test Plan For The Crude Butadiene C4 Category. American Chemistry Council, Olefins Panel, HPV Implementation Task Group. VA, USA.
Test Substance: (FT - TS)	25167-67-3 Butenes 68477-41-8 Distillate (Petroleum), Extractive C3-5 68955-28-2 Gases, (Petroleum) Light Steam Cracked, Butadiene Concentrate 68476-44-8 Hydrocarbons, >C3 68512-91-4 Hydrocarbons C3 – C4 Rich Petroleum Distillates 68187-60-0 Hydrocarbons, C4, Ethane-Propane Cracked 68476-52-8 Hydrocarbons, C4, Ethylene Manufactured By-Product 68956-54-7 Hydrocarbons C4, Unsaturated 69103-05-5 Hydrocarbons, C4-7, Butadiene Manufactured By-Product 64742-83-2 Naphtha, (Petroleum), Light Steam-Cracked
Conclusion: (FT - CL)	Based on the calculated K_{ow} values, products in this category can have a water solubility range of 424.1 to 732.4 mg/L. Based on the measured K_{ow} values, products in this category can have a water solubility range of 135.6 to 792.3 mg/L.
Reliability: (FT - RL)	(2) Reliable with restrictions The results include values estimated using calculated K_{ow} and experimental K_{ow} values available in the WSKOWWIN program and represent a potential water solubility range for products with the 10 CAS numbers listed under Test Substance.
Reference: (FT - RE)	Meylan, M., SRC 1994-1999. WSKOWWIN is contained in the computer program EPIWIN. 1999. Estimation Program Interface for Windows, version 3.04. Syracuse Research Corporation, Syracuse, NY, USA.
Other (source): (FT - SO)	American Chemistry Council, Olefins Panel

* Other TS is an option in the "test substance" pick list within the IUCLID data entry field for "water solubility". Selecting this option refers the reader to information in the "freetext" field for "test substance".

FT - Freetext
IUCLID fields include:
- RL - Reliability
- TC - Test Conditions
- RE - Reference
- RS - Results
- TS - Test Substance
- SO - Source
- CL - Conclusion

ENVIRONMENTAL FATE ROBUST SUMMARIES

Photodegradation (Direct)

Test Substance*:	Other TS
Method/Guideline:	Other: Technical discussion
Year (guideline):	Not applicable
GLP (Y/N):	Not applicable
Year (study performed):	Not applicable
Type (air, soil, water, other):	Not applicable
Light Source: **Light Spectrum:** • **Wave length value (upper/lower)**	Not applicable Not applicable
Relative Intensity:	Not applicable
Test Substance Spectrum:	Not applicable
Test Conditions: (FT - TC) • **Note: Concentration, temperature, test system type, replication, deviations from guideline or protocol**	Not applicable
Direct Photolysis:** **Results: half-life, % degradation, quantum yield**	**Summary** In the environment, photolysis will not significantly contribute to the degradation of chemicals in the Crude Butadiene C4 Category (C4 refers to a chemical with 4 carbons). The Crude Butadiene C4 Category includes two process streams: • **C4 Crude Butadiene** • **Butadiene Unit Heavy Ends** Ten CAS numbers (see Test Substance) identify products derived from these process streams. As discussed below, the reaction process involved in direct photolysis occurs when sufficient light energy excites a molecule to the degree that a structural transformation occurs. In general, products in this

	category do not contain component chemicals that will undergo direct photolysis. **The Crude Butadiene C4 Category** A process stream is a mixture of chemicals that arises from a chemical reaction or separation activity. Process streams containing 10 to 92% butadiene are referred to as "crude butadiene." The CAS numbers or streams in this category consist of complex mixtures of hydrocarbons. Most commercial products in this category have a carbon number distribution predominantly between C3 and C5. All of these streams contain significant levels of 1,3-butadiene and olefins, which is why this group is considered a category for purposes of the High Production Volume (HPV) Chemical Program, and designated Crude Butadiene C4. The definitions found in the TSCA Chemical Substance Inventory for the CAS numbers included in this group are vague with respect to composition. Therefore, it is possible to find that the same CAS number is correctly used to describe different streams (compositions) or that two or more different CAS numbers are used to describe the same stream (composition or process). Crude butadiene streams arise from production processes associated with ethylene manufacturing. More information on the Crude Butadiene C4 Category can be found in the American Chemistry Council, Olefins Panel test plan for this category (1). The plan is available on the U.S. Environmental Protection Agency website under the HPV Chemical Program. A brief description of the production and composition of the two process streams in this category are: • **C4 Crude Butadiene** is produced by the distillation of a condensed portion of cracked gas in an ethylene process. C4 Crude Butadiene typically contains 40% to about 60% 1,3-butadiene, but could contain between 10% and 82% butadiene. Other chemicals in this mixed stream are predominately chemicals containing 4 carbons. • **Butadiene Unit Heavy Ends** is produced by extractive distillation of cracked gas. The 1,3-butadiene content of this mixed stream ranges from 13% to 92%. Other chemicals in this mixed stream are predominately chemicals containing 4 carbons. Only three companies report isolating this stream which is more typically an un-isolated intermediate.

	Photolysis of Hydrocarbons The direct photolysis of an organic molecule occurs when it absorbs sufficient light energy to result in a structural transformation (2). The reaction process is initiated when light energy in a specific wavelength range elevates a molecule to an electronically excited state. However, the excited state is competitive with various deactivation processes that can result in the return of the molecule to a non excited state. The absorption of light in the ultra violet (UV)-visible range, 110-750 nm, can result in the electronic excitation of an organic molecule. Light in this range contains energy of the same order of magnitude as covalent bond dissociation energies (2). Higher wavelengths (e.g., infrared) result only in vibrational and rotational transitions, which do not tend to produce structural changes to a molecule. The stratospheric ozone layer prevents UV light of less than 290 nm from reaching the earth's surface. Therefore, only light at wavelengths between 290 and 750 nm can result in photochemical transformations in the environment (2). Although the absorption of UV light in the 290-750 nm range is necessary, it is not always sufficient for a chemical to undergo photochemical degradation. Energy may be re-emitted from an excited molecule by mechanisms other than chemical transformation, resulting in no change to the parent molecule. A conservative approach to estimating a photochemical degradation rate is to assume that degradation will occur in proportion to the amount of light wavelengths >290 nm absorbed by the molecule (3). Saturated hydrocarbons do not absorb light above 200 nm. Some characteristic absorbance maxima (λ_{max}) and associated molar absorptivities (ε) for selected unsaturated hydrocarbons are shown below (2):

<table>
<tr><td></td><td>
<table>
<tr><td rowspan="2">Hydrocarbon</td><td colspan="2">l below 290 nm</td></tr>
<tr><td>l_{max}</td><td>e</td></tr>
<tr><td>Ethylene</td><td>193</td><td>10,000</td></tr>
<tr><td>1,3-Butadiene</td><td>217</td><td>2,090</td></tr>
</table>
</td></tr>
<tr><td>Direct Photolysis**: (cont.)

Results: half-life, % degradation, quantum yield</td><td>Olefins with one double bond, two conjugated double bonds, or multiple un-conjugated bonds, which constitute the majority of the chemicals in the Crude Butadiene C4 Category, do not absorb appreciable light energy above 290 nm. The absorption of UV light to cause cis-trans isomerism about the double bond of an olefin occurs only if it is in conjugation with an aromatic ring (2).

Products in the Crude Butadiene C4 Category do not contain component molecules that will undergo direct photolysis. Therefore, this fate process will not contribute to a measurable degradative removal of chemical components in this category from the environment.

References
1. Olefins Panel, HPV Implementation Task Group. 2001. High Production Volume (HPV) Chemical Challenge Program Test Plan For The Crude Butadiene C4 Category. American Chemistry Council, Olefins Panel, HPV Implementation Task Group. Virginia, USA.
2. Harris, J. C. 1982. "Rate of Aqueous Photolysis," Chapter 8 in: W. J. Lyman, W. F. Reehl, and D. H. Rosenblatt, eds., Handbook of Chemical Property Estimation Methods, McGraw-Hill Book Company, New York, USA.
3. Zepp, R. G. and D. M. Cline. 1977. Rates of Direct Photolysis in the Aqueous Environment, Environ. Sci. Technol., 11:359-366.</td></tr>
<tr><td>Indirect Photolysis**:

• Results: type of sensitizer, concentration of sensitizer, rate constant, % degradation, half-life</td><td>Not applicable</td></tr>
<tr><td>Degradation Products**:

• Note: Identification, concentration</td><td>Unknown</td></tr>
</table>

Test Substance: (FT - TS)	25167-67-3 Butenes 68477-41-8 Distillate (Petroleum), Extractive C3-5 68955-28-2 Gases, (Petroleum) Light Steam Cracked, Butadiene Concentrate 68476-44-8 Hydrocarbons, >C3 68512-91-4 Hydrocarbons C3 – C4 Rich Petroleum Distillates 68187-60-0 Hydrocarbons, C4, Ethane-Propane Cracked 68476-52-8 Hydrocarbons, C4, Ethylene Manufactured By-Product 68956-54-7 Hydrocarbons C4, Unsaturated 69103-05-5 Hydrocarbons, C4-7, Butadiene Manufactured By-Product 64742-83-2 Naphtha, (Petroleum), Light Steam-Cracked
Conclusion: (FT - CL)	Not applicable
Reliability: (FT - RL)	Not applicable
Reference: (FT - RE)	American Chemistry Council, Olefins Panel. 2002. Hydrolysis: Crude Butadiene C4 Category. Rosslyn, VA, USA.
Other (source): (FT - SO)	American Chemistry Council, Olefins Panel

* Other TS is an option in the "test substance" pick list within the IUCLID data entry field for "photodegradation". Selecting this option refers the reader to information in the "freetext" field for "test substance".

** In IUCLID, provide addtional discussion if needed in the results freetext

FT - Freetext

IUCLID fields include:

- RL - Reliability
- TC - Test Conditions
- RE - Reference
- RS - Results
- TS - Test Substance
- SO - Source
- CL - Conclusion

Photodegradation (Indirect)

Test Substance*:	Other TS
Method/Guideline:	Calculated values using AOPWIN version 1.89, a subroutine of the computer program EPIWIN version 3.04
Year (guideline):	1999
GLP (Y/N):	Not applicable
Year (study performed):	Not applicable
Type (air, soil, water, other):	Not applicable
Light Source:	Sunlight
Light Spectrum: • **Wave length value (upper/lower)**	Natural sunlight
Relative Intensity:	1
Test Substance Spectrum:	Not applicable
Test Conditions: (FT - TC) • **Note: Concentration, temperature, test system type, replication, deviations from guideline or protocol**	Indirect photodegradation, or atmospheric oxidation potential, is based on the structure-activity relationship methods developed by R. Atkinson. Temperature: 25°C Sensitizer: OH radical Concentration of Sensitizer: $1.5\ E^{6}$ OH radicals/cm^3
Direct Photolysis:** **Results: half-life, % degradation, quantum yield**	Not applicable
Indirect Photolysis:** • **Results: type of sensitizer, concentration of sensitizer, rate constant, % degradation, half-life**	In the environment, organic chemicals emitted into the troposphere are degraded by several important transformation processes. The dominant transformation process for most compounds is the daylight reaction with hydroxyl (OH-) radicals (1,2). The rate at which an organic compound reacts with OH- radicals is a direct measure of its atmospheric persistence (3). AOPWIN estimates the rate constant for the atmospheric, gas-phase reaction between photochemically produced hydroxyl radicals and organic chemicals. The rate constants estimated by the program are then used to calculate atmospheric half-lives for organic compounds based upon

average atmospheric concentrations of hydroxyl radicals.

Since the reactions only take place in the presence of sunlight, the atmospheric half-lives are normalized for a 12-hour day.

Chemical	Calculated* half-life (hrs)	OH- Rate Constant (cm^3/molecule-sec)
Isobutane	52.6	$2.4 E^{-12}$
n-butane	48.8	$2.6 E^{-12}$
isobutylene	2.5	$51.7 E^{-12}$
cis-butene-2	2.3	$56.7 E^{-12}$
trans-butene-2	2.0	$64.3 E^{-12}$
butene-1	4.7	$27.4 E^{-12}$
1,3-butadiene	1.9	$66.6 E^{-12}$

* Atmospheric half-life values are based on a 12-hr day.

Commercial products in this category can have a carbon number distribution predominantly between C3 and C5. These products can contain significant levels of 1,3-butadiene and similar low molecular weight olefins, which is why they are considered a category for purposes of the High Production Volume Chemical Program, and designated Crude Butadiene C4.

The seven chemicals selected to represent the atmospheric half-life range of this category are C4 hydrocarbons that are common across the 10 CAS numbers listed under Test Substance. Crude butadiene category products arise from production processes associated with ethylene manufacturing. More information on the Crude Butadiene C4 Category can be found in the American Chemistry Council, Olefins Panel test plan for this category (4).

References:

1. Atkinson, R. 1988. Estimation of gas-phase hydroxyl radical rate constants for organic chemicals. *Environ. Toxicol. Chem*. **7**:435-442.
2. Atkinson, R. 1989. Kinetics and mechanisms of the gas-phase reactions of the hydroxyl radical with organic compounds. J. Phys. Chem. Ref. Data Monograph No. 1, Amer. Inst. Physics & Amer. Chem. Soc., NY.
3. Meylan, W.M. and P.H. Howard. 1993. Computer estimation of the atmospheric gas-phase reaction rate of organic compounds with hydroxyl radicals and ozone. *Chemosphere* **12**:2293-2299.
4. Olefins Panel, HPV Implementation Task Group. 2001. High Production Volume (HPV) Chemical Challenge Program Test Plan For The Crude Butadiene C4

	Category. American Chemistry Council, Olefins Panel, HPV Implementation Task Group. VA, USA.
Degradation Products:** • **Note: Identification, concentration**	Unknown
Test Substance: (FT - TS)	25167-67-3 Butenes 68477-41-8 Distillate (Petroleum), Extractive C3-5 68955-28-2 Gases, (Petroleum) Light Steam Cracked, Butadiene Concentrate 68476-44-8 Hydrocarbons, >C3 68512-91-4 Hydrocarbons C3 – C4 Rich Petroleum Distillates 68187-60-0 Hydrocarbons, C4, Ethane-Propane Cracked 68476-52-8 Hydrocarbons, C4, Ethylene Manufactured By-Product 68956-54-7 Hydrocarbons C4, Unsaturated 69103-05-5 Hydrocarbons, C4-7, Butadiene Manufactured By-Product 64742-83-2 Naphtha, (Petroleum), Light Steam-Cracked
Conclusion: (FT - CL)	Atmospheric oxidation vial hydroxyl radical can be a significant route of degradation for products in this category. Based on calculated values, products in this category can have an atmospheric half-life range of 1.9 to 52.6 hours as a result of indirect photolysis by hydroxyl radical attack.
Reliability: (FT - RL)	(2) Reliable with restrictions The results include values calculated using the AOPWIN program and represent a potential atmospheric half-life range for products with the 10 CAS numbers listed under Test Substance.
Reference: (FT - RE)	Meylan, M., SRC 1994-1999. AOPWIN is contained in the computer program EPIWIN. 1999. Estimation Program Interface for Windows, version 3.04. Syracuse Research Corporation, Syracuse, NY, USA.
Other (source): (FT - SO)	American Chemistry Council, Olefins Panel

* Other TS is an option in the "test substance" pick list within the IUCLID data entry field for "photodegradation". Selecting this option refers the reader to information in the "freetext" field for "test substance".
** In IUCLID, provide additional discussion if needed in the results freetext
FT - Freetext
IUCLID fields include:
RL - Reliability
TC - Test Conditions

RE - Reference
RS - Results
TS - Test Substance
SO - Source
CL - Conclusion

Hydrolysis (Stability in Water)

Test Substance*:	Other TS
Method/Guideline:	Other: Technical discussion
Year (guideline):	Not applicable
Type (test type): **GLP (Y/N):**	Not applicable Not applicable
Year (study performed):	Not applicable
Analytical Monitoring:	Not applicable
Test Conditions: (FT - TC) • **Note: Concentration preparation, vessel type, volume, replication, deviations from guideline or protocol**	Not applicable
Results: (FT - RS) **Units/Value:** • **Note: Analytical method, observations, half-lives by pH, degradation products**	Not applicable
Test Substance: (FT - TS)	25167-67-3 Butenes 68477-41-8 Distillate (Petroleum), Extractive C3-5 68955-28-2 Gases, (Petroleum) Light Steam Cracked, Butadiene Concentrate 68476-44-8 Hydrocarbons, >C3 68512-91-4 Hydrocarbons C3 – C4 Rich Petroleum Distillates 68187-60-0 Hydrocarbons, C4, Ethane-Propane Cracked 68476-52-8 Hydrocarbons, C4, Ethylene Manufactured By-Product 68956-54-7 Hydrocarbons C4, Unsaturated 69103-05-5 Hydrocarbons, C4-7, Butadiene Manufactured By-Product 64742-83-2 Naphtha, (Petroleum), Light Steam-Cracked
Conclusion: (FT - CL)	**Summary** In the environment, hydrolysis will not contribute to the

degradation of chemicals in the Crude Butadiene C4 Category (C4 refers to a chemical with 4 carbons). This category includes two process streams:

- **C4 Crude Butadiene**
- **Butadiene Unit Heavy Ends**

Ten CAS numbers (see Test Substance) identify products derived from these process streams. As discussed below, the chemicals in these streams are composed of carbon and hydrogen and are not amenable to hydrolysis because of their molecular structure and the chemical reaction required for this type of transformation to occur.

The Crude Butadiene C4 Category

A process stream is a mixture of chemicals that arises from a chemical reaction or separation activity. Process streams containing 10 to 92% butadiene are referred to as "crude butadiene." The CAS numbers or streams in this category consist of complex mixtures of hydrocarbons.

Most commercial products in this category have a carbon number distribution predominantly between C3 and C5. All of these streams contain significant levels of 1,3-butadiene and olefins, which is why this group is considered a category for purposes of the High Production Volume (HPV) Chemical Program, and designated Crude Butadiene C4.

The definitions found in the TSCA Chemical Substance Inventory for the CAS numbers included in this group are vague with respect to composition. Therefore, it is possible to find that the same CAS number is correctly used to describe different streams (compositions) or that two or more different CAS numbers are used to describe the same stream (composition or process).

Crude butadiene streams arise from production processes associated with ethylene manufacturing. More information on the Crude Butadiene C4 Category can be found in the American Chemistry Council, Olefins Panel test plan for this category (1). The plan is available on the U.S. Environmental Protection Agency website under the HPV Chemical Program. A brief description of the production and composition of the two process streams in this category are:

- **C4 Crude Butadiene** is produced by the distillation of a condensed portion of cracked gas in an ethylene process. C4 Crude Butadiene typically contains 40% to about 60% 1,3-butadiene, but could contain between 10% and 82% butadiene. Other chemicals in this mixed stream are

predominately chemicals containing 4 carbons.

- **Butadiene Unit Heavy Ends** is produced by extractive distillation of cracked gas. The 1,3-butadiene content of this mixed stream ranges from 13% to 92%. Other chemicals in this mixed stream are predominately chemicals containing 4 carbons. Only three companies report isolating this stream which is more typically an un-isolated intermediate.

Hydrolysis of Hydrocarbons as a Function of Molecular Structure

Hydrolysis of an organic molecule occurs when a molecule (R-X) reacts with water (H_2O) to form a new carbon-oxygen bond after the carbon-X bond is cleaved (2,3). Mechanistically, this reaction is referred to as a nucleophilic substitution reaction, where X is the leaving group being replaced by the incoming nucleophilic oxygen from the water molecule. The leaving group, X, must be a molecule other than carbon because for hydrolysis to occur, the R-X bond cannot be a carbon-carbon bond.

The carbon atom lacks sufficient electronegativity to be a good leaving group and carbon-carbon bonds are too stable (high bond energy) to be cleaved by nucleophilic substitution. Thus, hydrocarbons, including alkenes, are not subject to hydrolysis (3) and this fate process will not contribute to the degradative loss of chemical components in this category from the environment.

Under strongly acidic conditions the carbon-carbon double bond found in alkenes, such as those in the Crude Butadiene C4 Category, will react with water by an addition reaction mechanism (2). The reaction product is an alcohol. This reaction is not considered to be hydrolysis because the carbon-carbon linkage is not cleaved and because the reaction is freely reversible (3).

Chemicals that have a potential to hydrolyze include alkyl halides, amides, carbamates, carboxylic acid esters and lactones, epoxides, phosphate esters, and sulfonic acid esters (4). The chemicals in this category are primarily olefins that contain at least one double bond (alkenes). The remaining chemicals are saturated hydrocarbons (alkanes). These two groups of chemicals contain only carbon and hydrogen. As such, their molecular structure is not subject to the hydrolytic mechanism discussed above. Therefore, chemicals in the Crude Butadiene C4 Category have a very low potential to hydrolyze, and this degradative process will not contribute to their removal in the environment.

References

1. Olefins Panel, HPV Implementation Task Group. 2001. High

	Production Volume (HPV) Chemical Challenge Program Test Plan For The Crude Butadiene C4 Category. American Chemistry Council, Olefins Panel, HPV Implementation Task Group. VA, USA. 2. Gould, E.S. (1959), Mechanism and Structure in Organic Chemistry, Holt, Reinhart and Winston, New York, NY, USA. 3. Harris, J.C. (1982), "Rate of Hydrolysis," Chapter 7 in: W.J. Lyman, W.F. Reehl, and D.H. Rosenblatt, eds., Handbook of Chemical Property Estimation Methods, McGraw-Hill Book Company, New York, NY, USA. 4. Neely, W. B. 1985. Hydrolysis. In: W. B. Neely and G. E. Blau, eds. Environmental Exposure from Chemicals. Vol I., pp. 157-173. CRC Press, Boca Raton, FL, USA.
Reliability: (FT - RL)	Not applicable
Reference: (FT - RE)	American Chemistry Council, Olefins Panel. 2002. Hydrolysis: Crude Butadiene C4 Category. Rosslyn, VA, USA.
Other (source): (FT - SO)	American Chemistry Council, Olefins Panel

* Other TS is an option in the "test substance" pick list within the IUCLID data entry field for "hydrolysis". Selecting this option refers the reader to information in the "freetext" field for "test substance".

FT - Freetext

IUCLID fields include:

RL - Reliability
TC - Test Conditions
RE - Reference
RS - Results
TS - Test Substance
SO - Source
CL - Conclusion

Transport / Distribution (Fugacity)

Test Substance*:	Other TS
Method/Guideline:	Calculated according to Mackay Level I, EQC Model version 1.01
Year (guide line):	1997
Type (test type):	Not applicable
GLP:	Not applicable
Year (study performed):	Not applicable
Estimation Temperature:	25°C
Test Conditions: (FT - TC) • **Note: Concentration prep., vessel type, replication, test conditions.**	The EQC Level I is a steady state, equilibrium model that utilizes the input of basic chemical properties including molecular weight, vapor pressure, and water solubility to calculate distribution within a standardized regional environment. Physical properties input into the model are those calculated by the EPIWIN Estimation v 3.04 program (1) or supplied by the databases of experimental values contained with EPIWIN. Output data from the equilibrium model provides basic information on the potential distribution of chemicals between selected environmental compartments (i.e. air, water, soil, sediment, suspended sediment, biota). 1. EPIWIN. 1999. Estimation Program Interface for Windows, version 3.04. Syracuse Research Corporation, Syracuse, NY, USA.
Results: (FT - RS) **Units/Value:** • **Note: Deviations from protocol or guideline, analytical method.**	The following chemicals are representative of products in the Crude Butadiene C4 Category, which are complex, multi-constituent substances. The range of partitioning data for compone nt chemicals is an estimate of the partitioning behavior for category products. Calculated* Measured** Percent Distribution Percent Distribution Chemical Air Water Air Water Isobutane 99.99 0.01 99.99 0.01 n-butane 99.98 0.02 99.99 0.01 isobutylene 99.98 0.02 99.99 0.01 cis-butene-2 99.97 0.03 99.98 0.02 trans-butene-2 99.97 0.03 99.98 0.02

	butene-1 99.98 0.02 99.99 0.01 1,3-butadiene 99.97 0.03 99.97 0.03 * Distribution values determined using input data calculated by the EPIWIN program **Distribution values determined using input data supplied by the EPIWIN program experimental databases (EXPKOW.DB, EXP_MBVP.DB, and EXP_MBVP.DB) which contain more than 11,000 organic compounds with reliably measured values. Distribution of each chemical to each remaining compartment (soil, sediment, suspended sediment, biota) was calculated as less than 0.01%. Mobility in the environment is expected to be high due to the relatively high water solubility and high vapor pressure of these chemicals. Commercial products in this category can have a carbon number distribution predominantly between C3 and C5. These products can contain significant levels of 1,3-butadiene and similar low molecular weight olefins, which is why they are considered a category for purposes of the High Production Volume Chemical Program, and designated Crude Butadiene C4. The seven chemicals selected to represent the transport / distribution range of this category are C4 hydrocarbons that are common across the 10 CAS numbers (see Test Substance) and can represent a significant proportion of a product. Crude butadiene category products arise from production processes associated with ethylene manufacturing. More information on the Crude Butadiene C4 Category can be found in the American Chemistry Council, Olefins Panel test plan for this category (1). 1. Olefins Panel, HPV Implementation Task Group. 2001. High Production Volume (HPV) Chemical Challenge Program Test Plan For The Crude Butadiene C4 Category. American Chemistry Council, Olefins Panel, HPV Implementation Task Group. VA, USA.
Test Substance: (FT - TS)	25167-67-3 Butenes 68477-41-8 Distillate (Petroleum), Extractive C3-5 68955-28-2 Gases, (Petroleum) Light Steam Cracked, Butadiene Concentrate 68476-44-8 Hydrocarbons, >C3 68512-91-4 Hydrocarbons C3 – C4 Rich Petroleum Distillates 68187-60-0 Hydrocarbons, C4, Ethane-Propane Cracked 68476-52-8 Hydrocarbons, C4, Ethylene Manufactured By-

	Product 68956-54-7 Hydrocarbons C4, Unsaturated 69103-05-5 Hydrocarbons, C4-7, Butadiene Manufactured By-Product 64742-83-2 Naphtha, (Petroleum), Light Steam-Cracked
Conclusion: (FT - CL)	Products in the Crude Butadiene C4 Category are expected to distribute to air with a small percentage partitioning to water.
Reliability: (FT - RL)	(2) Reliable with restrictions The input data used to run the EQC Level I model include estimated values calculated by the EPIWIN program based on chemical structure, and experimental values supplied by the EPIWIN program databases. The partitioning data represent a potential distribution range for products with the 10 CAS numbers listed under Test Substance. Computer modeling is an accepted method of assessing environmental distribution of chemicals.
Reference: (FT - RE)	Mackay, D.A. DiGuardo, S. Paterson, and C. Cowan. EQC Model Version 1.01. 1997. Available from the Environmental Modeling Centre, Trent University, Canada.
Other (source): (FT - SO)	American Chemistry Council, Olefins Panel

* Other TS is an option in the "test substance" pick list within the IUCLID data entry field for "transport / distribution". Selecting this option refers the reader to information in the "freetext" field for "test substance".

FT - Freetext

IUCLID fields include:

- RL - Reliability
- TC - Test Conditions
- RE - Reference
- RS - Results
- TS - Test Substance
- SO - Source
- CL - Conclusion

Biodegradation

Test Substance*:	Other TS
Method/Guideline:	Other: Technical discussion
Year (guideline):	Not applicable
Type (test type): **GLP:**	Not applicable Not applicable
Year (study performed):	Not applicable
Inoculum:	Not applicable
Exposure Period:	Not applicable
Test Conditions: (FT - TC) • **Note: Concentration prep., vessel type, replication, test conditions.**	Not applicable
Results: (FT - RS) **Units/Value:** • **Note: Deviations from protocol or guideline, analytical method.**	Not applicable
Test Substance: (FT - TS)	25167-67-3 Butenes 68477-41-8 Distillate (Petroleum), Extractive C3-5 68955-28-2 Gases, (Petroleum) Light Steam Cracked, Butadiene Concentrate 68476-44-8 Hydrocarbons, >C3 68512-91-4 Hydrocarbons C3 – C4 Rich Petroleum Distillates 68187-60-0 Hydrocarbons, C4, Ethane-Propane Cracked 68476-52-8 Hydrocarbons, C4, Ethylene Manufactured By-Product 68956-54-7 Hydrocarbons C4, Unsaturated 69103-05-5 Hydrocarbons, C4-7, Butadiene Manufactured By-Product 64742-83-2 Naphtha, (Petroleum), Light Steam-Cracked
Conclusion: (FT - CL)	**SUMMARY** In the environment, biodegradation will not contribute significantly to the loss of chemicals in products from the

Crude Butadiene C4 Category (C4 refers to a chemical with 4 carbons). This category includes two process streams:

- **C4 Crude Butadiene**
- **Butadiene Unit Heavy Ends**

Ten CAS numbers (see Test Substance) identify products derived from these process streams. The products contain various chemicals composed of carbon and hydrogen. As discussed below, products in this category are gaseous. If they are released to the environment, their chemical components will partition primarily to the air where they can degrade rapidly by physicochemical reactions. It is far less likely that products from this category will partition to environmental compartments where they could be degraded by bacteria.

The Crude Butadiene C4 Category

A process stream is a mixture of chemicals that arises from a chemical reaction or separation activity. Process streams containing 10 to 92% butadiene are referred to as "crude butadiene." The CAS numbers or streams in this category consist of complex mixtures of hydrocarbons.

Most commercial products in this category have a carbon number distribution predominantly between C3 and C5. All of these streams contain significant levels of 1,3-butadiene and olefins, which is why this group is considered a category for purposes of the High Production Volume (HPV) Chemical Program, and designated Crude Butadiene C4.

The definitions found in the TSCA Chemical Substance Inventory for the CAS numbers included in this group are vague with respect to composition. Therefore, it is possible to find that the same CAS number is correctly used to describe different streams (compositions) or that two or more different CAS numbers are used to describe the same stream (composition or process).

Crude butadiene streams arise from production processes associated with ethylene manufacturing. More information on the Crude Butadiene C4 Category can be found in the American Chemistry Council, Olefins Panel test plan for this category (1). The plan is available on the U.S. Environmental Protection Agency website under the HPV Chemical Program. A brief description of the production and composition of the three process streams in this category are:

- **C4 Crude Butadiene** is produced by the distillation of a condensed portion of cracked gas in an ethylene process.

C4 Crude Butadiene typically contains 40% to about 60% 1,3-butadiene, but could contain between 10% and 82% butadiene. Other chemicals in this mixed stream are predominately chemicals containing 4 carbons.

- **Butadiene Unit Heavy Ends** is produced by extractive distillation of cracked gas. The 1,3-butadiene content of this mixed stream ranges from 13% to 92%. Other chemicals in this mixed stream are predominately chemicals containing 4 carbons. Only three companies report isolating this stream which is more typically an un-isolated intermediate.

Biodegradation of Hydrocarbons

Biodegradation is the use of a chemical by microorganisms as a source of energy and carbon. The parent chemical is broken down to simpler, smaller chemicals, which can be converted to inorganic forms such as carbon dioxide, nitrate, sulfate, and water.

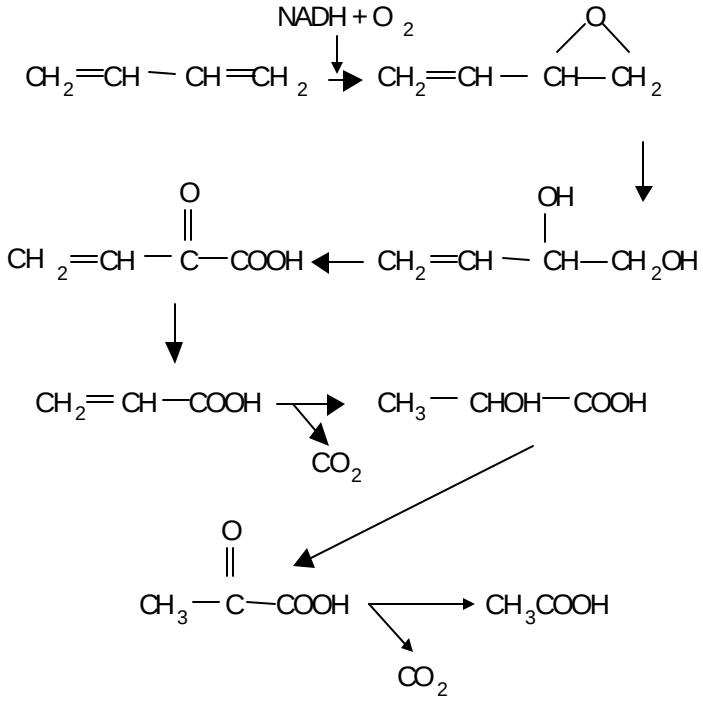
Products in the Crude Butadiene C4 Category are gaseous hydrocarbons, composed predominantly of chemicals with carbon numbers smaller than C5. However, the *Full-Range Butadiene Concentrates* process stream from this category, can contain hydrocarbons greater than C4. These chemicals when isolated individually are not gaseous, but relatively volatile liquids under most environmental conditions.

Several hydrocarbons as well as products that are mixtures of hydrocarbons with carbon numbers greater than C4 have been shown to biodegrade. If released to the environment, biodegradation of these chemicals will occur primarily in aquatic and terrestrial habitats. There is sufficient biodegradation data on hydrocarbons in this category that are greater than C4 to show that these chemicals have a potential to biodegrade to a great extent and not persist in the environment (see the *C5 Noncyclics, Low Benzene Naphtha, and High Benzene Naphtha* HPV Chemical Program test plans from the Olefins Panel of the American Chemistry Council, for specific data and a more detailed discussion of the biodegradability of selected hydrocarbons greater than C4.) The larger proportion of chemicals from this category are gaseous. Consequently, their availability to microbial degraders will be significantly limited.

Component chemicals from all three process streams in this category are simple hydrocarbons, the majority of which will partition primarily to the air where physical processes will contribute to their degradation [see the atmospheric oxidation potential (AOP) data (as mediated by hydroxyl radical

attack) for specific degradation rates of selected chemicals from this category; AOP data were developed for this category under the HPV Chemical Program]. All chemicals from this category that partition to the air are calculated to degrade rapidly due to physical processes and not persist. Because of the partitioning behavior of chemicals in this category, biodegradative processes will be less likely to contribute to their loss from the environment.

Products from the Crude Butadiene C4 Category do not lend themselves to being evaluated for biodegradability using standard experimental techniques because of their physical state. However, there is microbial metabolism information for one of the major chemicals, 1,3-butadiene, in this category that demonstrates that it can be biodegraded. Experimental studies to determine a catabolic pathway for 1,3-butadiene as mediated by a *Nocardia* sp. (3) resulted in the following proposed series of reactions:



The intermediary metabolic steps depicted above result in the production of acetic acid, CH3COOH, which can be further metabolized. In addition, 1,3-butadiene has been estimated to have an aerobic aquatic biodegradation half-life ranging from 1 to 4 weeks (2).

The potential biodegradability of some of the higher molecular weight components including benzene, toluene, xylene, ethylbenzene, and naphthalene has been summarized and metabolic pathways leading to their biodegradation have

	been described (4). These compounds have been shown to biodegrade to high extents such that if they were to partition to either a terrestrial or aqueous environment, they would be subject to biodegradative processes that would result in their removal from the environment. In summary, because the C4 and lighter chemical components of this category will partition to the air, physical degradative processes will dominate their fate. Data show that these chemicals are subject to rapid physical degradation. Chemical components of this category that are greater than C4 also have a potential to partition to the air to a great extent, where they will also degrade rapidly in a similar manner. However, they also have a potential to partition to aquatic and terrestrial environments where they are subject to biological processes that can result in their rapid biodegradation. Overall, products from this category and their component chemicals are expected to degrade rapidly in the environment and not persist. **References** 1. Olefins Panel, HPV Implementation Task Group. 2001. High Production Volume (HPV) Chemical Challenge Program Test Plan For The Crude Butadiene C4 Category. American Chemistry Council, Olefins Panel, HPV Implementation Task Group. Virginia, USA. 2. Howard, P.H., R.S. Boethling, W.F. Jarvis, W.M. Meylan, and E.M. Michalenko. 1991. Handbook of Environmental Degradation Rates. H.T. Printup Ed. Lewis Publishers, Chelsea, MI, USA. 3. Watkinson, R.J. and H.J. Somerville. 1976. The Microbial Utilization of Butadiene. Shell Research Limited, Sittingbourne Research Centre, Kent, UK. 4. van Agteren, M.H., S. Keuning, and D.B. Janssen. 1998. Handbook on Biodegradation and Biological Treatment of Hazardous Organic Compounds. Kluwer Academic Publishers. Boston, CT, USA.
Reliability: (FT - RL)	Not applicable
Reference: (FT - RE)	American Chemistry Council, Olefins Panel. 2002. Hydrolysis: Crude Butadiene C4 Category. Rosslyn, VA, USA.
Other (source): (FT - SO)	American Chemistry Council, Olefins Panel

* Other TS is an option in the "test substance" pick list within the IUCLID data entry field for "biodegradation". Selecting this option refers the reader to information in the "freetext" field for "test substance".
FT - Freetext
IUCLID fields include:

RL - Reliability
TC - Test Conditions
RE - Reference
RS - Results
TS - Test Substance
SO - Source
CL - Conclusion

HUMAN HEALTH ROBUST SUMMARIES

Acute Toxicity

Test Substance	
Remarks	Butadiene Concentrate, CAS# 68955-28-2 Gases (petroleum) light steam-cracked, butadiene conc. Approximately 45% 1,3-butadiene, 20% butanes, and 30% butenes.
Method	
Method/guideline followed	OECD 402.
Type (test type)	Acute inhalation.
GLP	Yes.
Year	1982.
Species/Strain	Rat/Fischer 344.
Sex	Males and females.
No. of animals per sex per dose	5/sex.
Vehicle	Not applicable.
Route of administration	Inhalation (gas).
Test Conditions	A group of ten rats (age: 12 weeks, weight: 143-234 grams) were exposed to 5,300 mg/m3 (2,331 ppm) of the test substance in air for four hours. Analytical chamber concentrations were determined by gas chromatography every 15 minutes during the exposure; a single particle size sample was taken to show the absence of aerosol. Body weights were recorded prior to exposure and 7 and 14 days post-exposure. Individual clinical observations were recorded pre-exposure and daily for 14 days post-exposure. The rats were sacrificed on the fourteenth day and a gross necropsy performed.
Results	
LC50	Rat LC50 (4 hour) = >5,300 mg/m3 (2,331 ppm)
Remarks	Observations noted following exposure were two male rats with respiratory sounds/wheezing or hyperexcitability and one female with minimal porphyrin around the eyes. All rats were normal from Days 2-14. No significant necropsy findings were reported, except one female with an ovary filled with red fluid. Body weight gains appeared normal.
Conclusions	
(study author)	No mortality or significant adverse effects were observed in rats exposed to 5,300 mg/m3 (2,331 ppm) of the test substance.
Data Quality	
Reliability	Reliable without restrictions. Guideline study.
References	Gulf Oil Chemicals Company (1982). Acute LC50 Inhalation Toxicity Test in Rats with Butadiene Feedstock. Unpublished report (Project #82-060).

Other	Robust Summary prepared by ExxonMobil Biomedical Sciences, Inc.
Last changed	19-Oct-99

Acute Toxicity

Test Substance	1,3-butadiene CAS# 106-99-0
Method	
Method/guideline followed	Other.
Type (test type)	Acute inhalation.
GLP	Pre-GLP.
Year	1969.
Species/Strain	Rat and mouse (strains not specified).
Sex	Not specified.
No. of animals per sex per dose	Not specified.
Vehicle	Not applicable.
Route of administration	Inhalation (gas).
Test Conditions	Age, number, and sex of test animals not specified. Number of groups and exposure concentrations not specified. Dynamic flow exposure system; no description of exposure chambers or conditions. Rats exposed four hours; mice exposed two hours. No post-exposure observation period - mortality study only. Exposure concentrations "controlled" by gas chromatography.
Results	
LC50 with confidence limits	Rat LC50 (4 hour) = 285 mg/L (219-370 mg/L $p \leq 0.05$) Mouse LC50 (2 hour) = 270 mg/L (251-290 mg/L $p \leq 0.05$)
Remarks	No clinical observations or necropsy findings reported. Objective of study was to determine hydrocarbon concentrations in various tissues at lethal exposure concentrations.
Conclusions	
(study author)	LC50 value reported to be 285 mg/L (129,000 ppm) in rats, 270 mg/L (122,000 ppm) in mice.
Data Quality	
Reliability	Not assignable. Lethality study only; insufficient experimental detail to assess quality.
References	Shugaev, B.B. (1969) Concentrations of Hydrocarbons in Tissues as a Measure of Toxicity. Arch. Environ. Health 18:878-882.
Other	Robust Summary Prepared by ExxonMobil Biomedical Sciences, Inc.
Last changed	13-Oct-99

Acute Toxicity

Test Substance	Butadiene Concentrate, CAS# 68955-28-2 Gases (petroleum) light steam-cracked, butadiene conc. Approximately 67% 1,3-butadiene, 30% butenes, 2% 1,2-butadiene
Method	
Method/guideline followed	Other.
Type (test type)	Irritation screen in rabbits.
GLP	Yes.
Year	1985.
Species/Strain Sex	Rabbit (New Zealand White). 1 male, 1 female.
Vehicle	Not applicable.
Route of administration	Eye and skin.
Remarks For Test Conditions	Two young adult rabbits were evaluated for eye and skin irritation. The test substance was dispensed immediately prior to dosing into a flask packed in dry ice. On the first treatment day, 0.1mL of the test substance was instilled into one eye of each rabbit. Irritation was scored at 24, 48, and 72 hours. The untreated eye served as the control. Twenty-four hours after treatment of the eye, 0.1mL of the test substance was applied to the skin of the rabbits and occluded with a rubber dam. The test sites were evaluated 1, 3, and 7 days after dosing.
Results	
Remarks	The eye irritation scores were 0 at all observation intervals. The treated skin sites were virtually free of irritation at all observation intervals.
Conclusions	
(study author)	The test substance is estimated not to be irritating to the eye or skin.
Data Quality	
Reliability	Reliable with restrictions. Screening study.
References	Mobil Environmental and Health Sciences Laboratory (1985). Irritation Screen of Butadiene Concentrate in Albino Rabbits, Unpublished report (Study No. 41652).
Other	Robust Summary prepared by ExxonMobil Biomedical Sciences, Inc.
Last changed	24-Oct-99

Genetic Toxicity - *in vitro*

Test Substance	
Test substance	1,3-butadiene CAS# 106-99-0
Method	
Method/guideline followed	No data.
Type	Reverse mutation assay (Ames *Salmonella* test).
System of testing	Bacterial.
GLP	No data.
Year	1990.
Species/Strain	Salmonella typhimurium/TA97, TA98, TA100, TA1535.
Metabolic activation	With and without.
Species and cell type	Rat, mouse, and human liver S9 fraction.
Quantity	0.8 and 4.0 mg protein/plate.
Induced or not induced	Arochlor 1254-induced and uninduced rat, mouse, and human S9.
Concentrations tested	0, 30, 40, 50, and 60% butadiene in air.
Statistical Methods	Not specified.
Remarks for Test Conditions	Concentrations of butadiene gas were metered into specially constructed treatment chambers holding the agar plates overlaid with the bacteria and activation system. Actual gas concentrations were determined by gas chromatography before and after the 48 hour exposure period. Different treatment chambers were used for each activation system and for the non-activated treatment. S9 preparations were made according to the procedure of Ames *et al.* (1975).
Results	1,3-Butadiene (BD) induced revertants only in strain TA1535. Mouse S9 showed slightly higher activity than the uninduced rat or human S9 at 30% 1,3-butadiene in air. At concentrations greater than 30%, the number of revertants decreased in the presence of rat or human S9. Results from the human S9-activated treatments did not differ substantially from those of the non-activated treatments. Arochlor 1254-induced rat S9 gave similar results as mouse S9 (uninduced). Since the response was weak, the S9 concentration was increased from 0.8 mg/plate to 4.0 mg/plate. Increasing the concentration of Arochlor 1254-induced rat S9 had no effect on the number of revertants; slightly more revertants were observed using 4.0 than 0.8 mg/plate of uninduced rat S9.
Conclusions	
(study author)	*Salmonella typhimurium* reverse gene mutation (Ames) tests of 1,3-butadiene using strains TA1535, TA97, TA98, and TA100 and employing rat, mouse, and human liver S9 metabolic systems were barely 2-fold above background only in strain TA1535 at 30% butadiene in air with induced and uninduced rat S9 and mouse S9 (uninduced). In general, 1,3-butadiene was a weak *in vitro* genotoxin.
Data Quality	
Reliabilities	Reliable without restrictions. Comparable to guideline study.
Reference	Arce G.T., Vincent D.R., Cunningham M..J, Choy W.N., and Sarrif

	A.M. (1990). *In vitro* and *in vivo* genotoxicity of 1,3-butadiene and metabolites. Environ. Health Perspect. 86:75-8.
Other	Robust Summary Prepared by ExxonMobil Biomedical Sciences, Inc.
Last changed	18-Oct-99

Genetic Toxicity - *in vitro*

Test Substance	
Test substance	Butadiene Concentrate, CAS# 68955-28-2. Gases (petroleum) light steam-cracked, butadiene conc. Approximately 45% 1,3-butadiene, 20% butanes, and 30% butenes.
Method	
Method/guideline followed	OECD 482.
Type	Unscheduled DNA Synthesis (UDS).
System of testing	Primary hepatocytes derived from Fischer 344 rats.
GLP	Yes.
Year	1984.
Metabolic activation	No.
Concentrations tested	0, 1000, 5000, 10000, and 20000 ppm.
Control groups and treatment	Negative = air only; positive = 2-acetylaminofluorene (0.2ug/mL).
Statistical Methods	Group means and standard deviations for number of viable cells and nuclear grain counts. The test substance was considered positive if the mean nuclear grain count exceeded the negative control by at least 6 grains per nucleus and the negative control did not exceed 5.
Remarks for Test Conditions	Primary hepatocytes were derived from freshly perfused rat liver (1 male, 10 weeks age, 226 grams body weight). Cultures were seeded with approximately 10^5 cells/mL on Day 1. Three cultures per group were exposed to ^{3}H-thymidine and the test substance for 18-20 hours. The culture flasks were placed in sealed dessicator jars for the exposure period, and the test substance added by injection via a 50cc syringe. Cells growing on coverslips were fixed on Day 2. On Day 3 the slides were dipped in autoradiograph emulsion and stored in the dark at 2-8^{o}C. The autoradiographs were developed and stained on Day 21.
Results	A separate range-finding study was conducted to establish levels of cytotoxicity based on relative cell viability. The test substance was toxic to primary hepatocytes at 10000 ppm where 64% relative viability was observed following 18 hour exposure. At 20000 ppm, the relative viability was 57%. In the UDS study, both positive and negative control groups gave expected responses. A weak positive response was observed at 20000 ppm (7.74 nuclear grain counts vs. 1.24 in the air control vs. 107.13 in the positive control). The 1000, 5000, and 10000 ppm groups were also slightly increased (4.29-5.14) from the air control but less than the criteria for a significant response.
Conclusions (study author)	Cytotoxicity was observed at 10000 ppm. Increased unscheduled DNA synthesis was observed at 20000 ppm.
Data Quality	
Reliabilities	Reliable without restrictions. Guideline study.
Reference	Gulf Oil Chemicals Company (1984). Hepatocyte Primary Culture/DNA Repair Test of Butadiene Feedstock, Unpublished report (Project# 2073).
Other	Robust Summary Prepared by ExxonMobil Biomedical Sciences,

	Inc.
L*ast changed*	18-Oct-99

Genetic Toxicity - *in vitro*

Test Substance	
Test substance	Butadiene Concentrate, CAS# 68955-28-2 Gases (petroleum) light steam-cracked, butadiene conc. Approximately 45% 1,3-butadiene, 20% butanes, and 30% butenes.
Method	
Method/guideline followed	Other.
Type	Mammalian cell transformation test.
System of testing	BALB/3T3-A31-1-1 cells.
GLP *Year*	Yes. 1983.
Metabolic activation	No.
Concentrations tested	0, 1000, 5000, 10000, and 20000 ppm.
Control groups and treatment	Negative = air only; positive = 3-methylcholanthrene (1.0 ug/mL).
Statistical Methods	Group means and standard deviations for number of viable cells, cloning efficiency, and transformed foci per culture. The test substance was considered positive if there was a two-fold increase in foci compared to the negative control group.
Remarks for Test Conditions	Each treatment group consisted of 12 flask cultures for cell transformation seeded with 10000 cells and 2 plate cultures for cloning efficiency with 250 cells. The cultures were placed in sealed dessicator jars and exposed to the test substance for two days. The test substance was added to the jars by injection via a 50cc syringe and samples of the exposure atmosphere were analyzed by gas chromatography. The mediums were changed on Day 4 and then weekly. Plate cultures were fixed and stained on Day 8 and flask cultures on Day 29. Foci in transformation cultures were counted and examined microscopically to determine type.
Results	Cloning efficiency was used as a measure of toxicity under culture conditions. Toxicity was observed at 5000 ppm where a relative cloning efficiency of 53.8% was observed. The negative and positive control gave expected responses for transformation. The response for the test substance was not increased from the negative control group at any level tested.
Conclusions	
(study author)	The test substance was negative for cell transformation.
Data Quality	
Reliabilities	Reliable without restrictions. Comparable to draft OECD guideline.
Reference	Gulf Oil Chemicals Company (1983). BALB/3T3 Transformation Test Using Butadiene Feedstock, Unpublished report (Project# 2074).
Other	Robust Summary Prepared by ExxonMobil Biomedical Sciences, Inc.
Last changed	18-Oct-99

Genetic Toxicity - *in vitro*

Test Substance	
Remarks	Butadiene Concentrate, CAS# 68955-28-2 Gases (petroleum) light steam-cracked, butadiene conc. Approximately 67% 1,3-butadiene, 30% butenes, 2% 1,2-butadiene.
Method	
Method/guideline followed	No data.
Type	Reverse mutation assay (Ames *Salmonella* test).
System of testing	Bacterial.
GLP Year	Yes. 1985.
Species/Strain	Salmonella typhimurium/ TA98, TA100, TA1535, TA1537, TA1538.
Metabolic activation	With and without.
Species and cell type	Rat liver S9 fraction.
Quantity	0.6 mL.
Induced or not induced	Arochlor 1254-induced.
Concentrations tested	25, 50, 75, or 100 uL.
Statistical Methods	The test substance was considered mutagenic if it produced a dose-related two-fold increase in mean revertant value compared to the negative control.
Remarks for Test Conditions	The test substance was stored in a dry ice/ethanol slurry to prevent loss of volatile components and dosed by microdispenser into sterile septa-capped culture tubes. Sodium phophate buffer or S-9/bacteria mix was injected through the septa into the tubes containing the test substance and pre-incubated for 20 minutes at 37°C. After the pre-incubation period, the contents of the tubes were overlayed on agar and incubated for 48 hours at 37°C. Revertant colonies were counted by automatic colony counter. Positive control chemicals were: 2.0 ug 2-aminoanthracene, 15.0 ug 9-aminoacridine, 20.0 ug 2-nitrofluorene, and 5.0 ug N-methyl-N-nitro-N-nitrosoguanidine, in 50 µl DMSO per plate.
Results	A preliminary toxicity/initial mutagenicity assay was conducted over a range of 10 to 500 µl per plate in two strains (TA100 and TA1537) with and without S-9. Toxicity was exhibited at ≥75uL in TA100, and ≥100uL in TA1537. Some inconsistencies in toxicity with increasing dose level were noted that were attributed to the volatility of the test substance. Based on the toxicity data, the test substance was tested in the pre-incubation mutagenicity assay at volumes of 25, 50, 75, and 100 µl per plate. None of the five strains with or without induced rat liver S-9 exhibited reversion frequencies substantially different from spontaneous controls in this assay.
Conclusions	
(study author)	The test substance was not considered a mutagen with or without metabolic activation in this test system.
Data Quality	

Reliabilities	Reliable without restrictions. Comparable to guideline study.
Reference	Mobil Environmental and Health Sciences Laboratory (1985). An Ames Salmonella/Mammalian Microsome Mutagenesis Assay For Determination of Potential Mutagenicity of Butadiene Concentrate, Unpublished report (Study No. 41653).
Other	Robust Summary Prepared by ExxonMobil Biomedical Sciences, Inc.
Last changed	24-Oct-99

Genetic Toxicity - *in vitro*

Test Substance	
Remarks	Butadiene Concentrate, CAS# 68955-28-2 Gases (petroleum) light steam-cracked, butadiene conc. Approximately 67% 1,3-butadiene, 30% butenes, 2% 1,2-butadiene.
Method	
Method/guideline followed	Other.
Type	Mouse lymphoma mutagenesis assay.
System of testing	Mammalian cell.
GLP Year	Yes. 1985.
Species/Strain	Mouse lymphoma cells/ L5178Y (TK+/-; subclone 3.7.2C).
Metabolic activation	With and without.
Species and cell type	Rat liver S9 fraction.
Quantity	4.0 mL.
Induced or not induced	Arochlor 1242/1254-induced.
Concentrations tested	Nonactivated assays: 10.0, 12.5, 15.0, 17.5, 20.0, 22.5, 25.0, 27.5, 30.0, 35.0 40.0, or 45.0 uL/mL media. S-9 activated assays: 2.5, 5.0, 7.5, 10.0, 12.5, 15.0, 17.5, 20. 0, 22.5, or 25.0 uL/mL.
Statistical Methods	The test substance was considered mutagenic if it produced a dose-related or toxicity-related two-fold increase in average mutant frequency compared to the negative controls, at concentrations exhibiting accepta ble total growths (10% or greater).
Remarks for Test Conditions	The positive control chemical for the S-9 activated assays was 7, 12-dimethylbenz[a]anthracene (DMBA) at 2.5 and 5.0 ug/mL, and ethylmethane sulfonate (EMS) for the nonactivated assays at 0.5 and 1.0 uL/mL. An initial toxicity assay was performed with and without activation at concentrations ranging from 10 to 100 uL/mL. The dosing regimen for the mutagenesis assay was designed to produce 10-90% lethality. Six mLs of cell suspension (10^6 cells/mL) were exposed for 3 hours to the test or positive control substances. An expression period of 2 days followed with determinations of cell population densities and growth. Cultures selected for mutant analysis and cloning efficiencies were incubated for 10-12 days.
Results	Without activation, mutant frequencies and total number of mutants were significantly increased at the two highest concentrations (20.0 and 22.5 uL/mL). Although total growth was very low (5.1% and 5.5%), these levels were considered mutagenic since there was no reduction in cloning efficiency. There were no significant differences in mutant frequency for the S-9 activated cultures.
Conclusions	
(study author)	The test substance induced a significant increase in mutant frequency of mouse lymphoma cells without metabolic activation, but was evaluated as non-mutagenic in the presence of S-9 activation.
Data Quality	

Reliabilities	Reliable without restrictions. Comparable to guideline study.
Reference	Mobil Environmental and Health Sciences Laboratory (1985). Evaluation of the Mutagenic Potential of Butadiene Concentrate in the Mouse Lyphoma (L5178Y/TK+/-) Mutagenesis Assay, Unpublished report (Study No. 41654).
Other	Robust Summary Prepared by ExxonMobil Biomedical Sciences, Inc.
Last changed	24-Oct-99

Genetic Toxicity - *in vivo*

Test Substance	
Remarks	1,3-butadiene CAS# 106-99-0
Method	
Method/guideline followed Type	Other. Mammalian erythrocyte micronucleus assay.
GLP	No data.
Year	1994.
Species	Rat and mouse.
Strain	Rat: Wistar. Mouse: CB6F1
Sex	Rat: Male. Mouse: Female.
Route of administration	Inhalation (gas).
Doses/concentration levels	0, 50, 200, or 500 ppm.
Exposure period	6 hours/day for 5 days.
Statistical methods	Student's two-tailed t-test for differences between groups.
Remarks for Test Conditions.	Twenty female CB6F1 mice (approximately 25g, 8-10 weeks old) and ten male Wistar rats (300-350g, 10 weeks old) per group were exposed for 5 days, 6 h/day 0, 50, 200, or 500 ppm of 1,3-butadiene (BD) by inhalation. An additional high concentration group of mice was exposed to 1300 ppm. Exposure concentrations were monitored by infrared spectroscopy (rats) and gas chromatography (mice). The animals were sacrificed 1 day after the last exposure and smears of blood and bone marrow erythrocytes were prepared and stained.
Results	In the rats, no effects on micronuclei frequencies were observed either in the peripheral blood or bone marrow at all exposure levels. A slight toxic effect in rat bone marrow cells (decreased polychromatic/normochromatic ratio) was observed at the 500 ppm level. In the mice, a clear dose-dependent increase in micronuclei frequency was observed in both blood and bone marrow cells at all exposure levels tested.
Conclusions	
(study author)	1,3-butadiene was active in inducing micronuclei in peripheral blood and bone marrow erythrocytes in mice at levels $\geq$50 ppm, but not in rats. The genotoxic effects observed in this study parallel the species differences observed in cancer studies.
Data Quality	
Reliabilities	Reliable without restrictions. Comparable to guideline study.
References	Autio, K., Renzi, L., Catalan, J., Albrecht, O.E., and Sorsa, M. (1994). Induction of Micronuclei in Peripheral Blood and Bone Marrow Erythrocytes of Rats and Mice Exposed to 1,3-Butadiene by Inhalation. Mut. Res. 309:315-320.
	Robust Summary Prepared by ExxonMobil Biomedical Sciences, Inc.
Last changed	25-Oct-99

Genetic Toxicity - i*n vivo*

Test Substance	
Remarks	Butadiene Concentrate, CAS# 68955-28-2 Gases (petroleum) light steam-cracked, butadiene conc. Approximately 45% 1,3-butadiene, 20% butanes, and 30% butenes.
Method	
Method/guideline followed	OECD 474
Type	Mammalian erythrocyte micronucleus test
GLP	Yes
Year	1984
Species	Mouse
Strain	Crl:CD-1 BR Swiss
Sex	Male and female
Route of administration	Inhalation (gas)
Doses/concentration levels	10,780; 20,671; 35,430 ppm
Exposure period	2 hours/day for 2 consecutive days
No. of animals per dose	10/sex/group
Control groups and treatment	10/sex negative (air) control; 5/sex positive control (cyclophosphamide, 75 mg/kg intraperitoneal injection)
Statistical methods	Group mean body weights, total polychromatic erythrocytes (PCEs), normochromatic erythrocytes (NORMs), PCEs with micronuclei, and NORMs with micronuclei were compared by t-test ($p<0.05$ = positive).
Remarks for Test Conditions.	Mice were 11 weeks old and 25-42 grams weight at study initiation. Test and control substances were administered on Days 1 and 2. Exposure concentrations determined by gas chromatography. Animals were observed daily and body weights were recorded on Days 1, 3, and 4. Five mice/sex/group were sacrificed on Days 3 and 4 and bone marrow smears prepared; positive controls (5/sex) were sacrificed on Day 3 only.
Results	No mice died during the study; the only clinical observations were an apparent unconsciousness during exposure. There were no significant body weight differences. The negative and positive control groups produced negative and positive resulats, respectively. Mice in the exposed groups showed increased micronuclei formation at all levels in both sexes. Females were statistically increased from control at all levels on Day 3 and at 20,671 ppm and 35,430 ppm on Day 4; males were significantly increased only at 35,430 ppm on both days. There was no significant change in the PCE/NORM ratio in any group.
Conclusions	
(study author)	The test material produced an increased frequency of micronucleated erythrocytes in the bone marrow of mice at all levels tested.
Data Quality	
Reliabilities	Reliable without restrictions. Guideline study.
References	Gulf Oil Chemicals Company (1984). Micronucleus Test in Mouse Bone Marrow: Butadiene Feedstock Administered by

	Inhalation For 2 Hours/Day For 2 Days, Unpublished report (Project #2014).
Other	Robust Summary Prepared by ExxonMobil Biomedical Sciences, Inc.
Last changed	13-Oct-99

Repeated Dose Toxicity

Test Substance	
Remarks	1,3-butadiene, CAS# 106-99-0 Rubber grade, containing 0.02% t-butyl catechol; purity ≥98.94%.
Method	
Method/guideline followed	Other
Test type	14-week inhalation study
GLP	Yes
Year	1977
Species	Mouse
Strain	B6C3F1
Route of administration	Inhalation (gas)
Duration of test	14 weeks
Doses/concentration levels	0, 625, 1250, 2500, 5000, or 8000 ppm
Sex Exposure period	10 male, 10 female per group 6 hours/day
Frequency of treatment	5 days/week, total of 63 or 64 exposures
Control group and treatment	10 male, 10 female, air-only exposed
Post exposure observation period	Not applicable
Statistical methods	Group means and standard deviations calculated for body weights.
Test Conditions	Groups of 10 mice/sex /group (4-5 weeks age at study initiation) were exposed to various levels of 1,3-butadiene for 6 hrs/day, 5 days/week for 14 weeks (64 exposures). Because four male mice in the high exposure group died by day 4, another 2 groups of 10 male mice each were restarted (control and 8000 ppm). Mice were observed once daily for morbidity and mortality; moribund animals were sacrificed. Body weights were recorded weekly. At the end of the 95 or 93-day (restart) studies, surviving mice were sacrificed. Necropsies were performed and tissues preserved. Histopathologic examinations were performed on all controls, high exposure (8000 ppm), and early deaths.
Results	
NOAEL (NOEL)	1250 ppm.
LOAEL (LOEL)	2500 ppm, based on reduced body weight gains.
Remarks	Six of ten males and 1/10 females exposed at 8000 ppm, 6/10 males and 1/10 females at 5000 ppm, and 1/10 males at 2500 or 1250 ppm died prior to study termination or were sacrificed in a moribund condition. Body weight gains were decreased in males at 2500, 5000, and 8000 ppm, and at 5000 and 8000 ppm in the females. No exposure-related histopathologic effects were observed in the high (8000 ppm) group.
Conclusions	Based on the results of this study, exposure levels of 625 and 1250 ppm were selected for a 2-year carcinogenicity study in

	mice based on reduced body weight gains and mortality in higher exposure groups.
Data Quality	
Reliabilities	Reliable with restrictions. Acceptable, well-documented study report but deficient by current guidelines. No organ weights, hematology or clinical chemistry evaluations were performed.
References	National Toxicology Program, Toxicology and Carcinogenesis Studies of 1,3-Butadiene (CAS No. 106-99-0) in B6C3F1 Mice (Inhalation Studies), NTP Technical Report Series No. 288, NIH Publication 84-2544 (1984).
Other	Robust Summary Prepared by ExxonMobil Biomedical Sciences, Inc.
Last changed	8-Dec-99

Repeated Dose Toxicity

Test Substance	
Remarks	1,3-butadiene, CAS# 106-99-0 Purity >99.2%, containing 120 ppm t-butyl catechol.
Method	
Method/guideline followed	Other.
Test type	13-week inhalation study.
GLP	No data.
Year	1977.
Species	Rat.
Strain	CD (Sprague-Dawley).
Route of administration	Inhalation (gas).
Duration of test	14 weeks.
Doses/concentration levels	0, 1000, 2000, 4000, or 8000 ppm.
Sex	40 male, 40 female per group.
Exposure period	6 hours/day.
Frequency of treatment	5 days/week for 13 weeks.
Control group and treatment	40 male, 40 female, exposed to filtered air only.
Post exposure observation period	Not applicable.
Statistical methods	Analysis of variance for body weights, food consumption, urinalysis, hematology, clinical chemistry, organ weights.
Test Conditions	Groups of 40 rats/sex /group (approx. 5 weeks age at study initiation) were exposed to various levels of 1,3-butadiene for 6 hrs/day, 5 days/week for 13 weeks. All animals were observed daily; individual body weights and food consumption were recorded weekly. Interim sacrifices of 10 rats/sex/group were performed after 2 and 6 weeks of exposure. Three urine samples were obtained from each animal during the 1-2 weeks prior to sacrifice. Blood samples were collected from all rats prior to the 2, 6, and 13 week sacrifices. Brain cholinesterase activity was measured using half the brain of 5 rats/sex/group at the 2 and 6-week sacrifices and all rats at the terminal sacrifice. Organ weights were recorded for the adrenals, brain, gonads, heart, kidneys, liver, lung, pituitary, spleen, and thyroid. Necropsies were performed and tissues preserved. Histopathologic examinations were performed on all control and high exposure (8000 ppm) tissues.
Results	
NOAEL (NOEL)	8000 ppm.
LOAEL (LOEL)	>8000 ppm.
Remarks	Increased salivation was observed in the females after 8 weeks exposure and decreased grooming (stained fur) in the males after 10 weeks. No other exposure-related conditions were observed. Male rats showed slight (non-statistically significant) reductions in body weight gains compared to the controls; female body weights at 1000 and 4000 ppm were statistically higher than the controls.

	Neuromuscular function tests using a modified rotating cone gave some random group differences, but were not considered exposure-related. There were no toxicologically significant differences in hematology, blood chemistry, brain cholinesterase measurements, or urine analysis. Organ weight and organ to brain weight ratios showed some scattered statistically significant differences among the groups but did not indicate any treatment-related effects. Microscopic examination of the tissues of the exposed rats showed a similar incidence and severity of histopathologic findings to the control group.
Conclusions	
(study author)	Rats exposed to butadiene gas at concentrations up to 8000 ppm showed no significant effects related to exposure.
Data Quality	
Reliabilities	Reliable without restrictions. Comparable to guideline study.
References	Crouch, C.N., Pullinger, D.H., and Gaunt, I.F. (1979) Inhalation Toxicity Studies With 1,3-butadiene - 2. 3 Month Toxicity Study in Rats. Am. Ind. Hyg. Assoc. J. 40:796-802.
Other	Robust Summary Prepared by ExxonMobil Biomedical Sciences, Inc.
Last changed	18-Oct-99

Repeated Dose Toxicity

Test Substance	
Remarks	Butadiene feedstock, CAS# 68955-28-2 Gases (petroleum) light steam-cracked, butadiene conc. Approximately 45% 1,3-butadiene, 20% butanes, and 30% butenes.
Method	
Method/guideline followed	Other.
Test type	9-day inhalation study.
GLP	Yes
Year	1982
Species	Rat
Strain	Fischer 344
Route of administration	Inhalation (gas)
Duration of test	12 days (9 exposures)
Doses/concentration levels	0, 2500, and 25100 mg/m3 (0, 1110, and 11140 ppm)
Sex	5 male, 5 female per group.
Exposure period	6 hours/day.
Frequency of treatment	9 exposure days
Control group and treatment	5 male, 5 female, exposed to air only.
Post exposure observation period	Not applicable.
Statistical methods	Bartlett's test and analysis of variance for body and organ weights. If the Bartlett's test indicated homogeneity, Dunnett's test was also performed; if non-homogeneous, a modified t-test was done.
Remarks for Test Conditions	Three groups of 5 rats/sex /group (8 weeks age and 120-198 grams at study initiation) were exposed to 0, 2500, or 25100 mg/m3 of the test substance for 6 hrs/day for a total of 9 exposures. The exposure regimen was 5 days of exposure , 2 days off, 4 days of exposure, then one day for the terminal sacrifice (12 days). Analytical chamber concentrations were determined by gas chromatography, 5 to 16 times per day in the low and high exposure chambers or approximately every 1.5 hours for the control chamber. A particle size sample was performed once daily for each exposure chamber to confirm the absence of aerosol. Individual animal observations were performed twice daily on exposure days and once daily on non-exposure days. Body weights were recorded prior to the first exposure and on Days 1, 7, and 12. Blood samples were obtained from all rats prior to sacrifice on Day 12. A gross necropsy was performed and organ weights recorded for the brain, heart, kidneys, liver, lung, and spleen. These organs plus the testes and ovaries were preserved and examined microscopically.
Results	
NOAEL (NOEL) LOAEL (LOEL)	11140 ppm >11140 ppm
Remarks	Most rats in both exposure groups appeared normal throughout

Conclusions	the study. Nasal discharge was observed in some rats of both groups, and at a greater incidence in the high exposure group. There were no statistically significant differences between the control and exposed groups for mean body weight, organ weight, hematology, or blood chemistry values. There were no exposure-related histopathologic changes in any of the organs and tissues examined.
(study author)	The 9-day repeated inhalation exposure of up to 11140 ppm (25100 mg/m3) resulted in no significant adverse effects in rats.
Data Quality	
Reliabilities	Reliable without restrictions. Comparable to guideline study (OECD 412).
References	Gulf Oil Chemicals Company (1983). Nine-day Repeated Dose Inhalation Study in Rats Using Butadiene Feedstock, Unpublished report (Project #82-090). (1983). Gulf Life Sciences Center, Pittsburgh PA
Other	Robust summary prepared by ExxonMobil Biomedical Sciences, Inc.
Last changed	19-Oct-99

Developmental Toxicity/Teratogenicity

Test Substance	
Remarks	1,3-butadiene, CAS# 106-99-0 Purity 99.88%
Method	
Method/guideline followed	OECD 414.
Test type	Developmental toxicity (teratogenicity) study.
GLP	Yes.
Year	1987.
Species	Mouse.
Strain	CD-1 (Swiss).
Route of administration	Inhalation (gas).
Concentration levels	0, 40, 200, or 1000 ppm.
Sex	18-22 pregnant females per group.
Exposure period	Days 6-15 of gestation.
Frequency of treatment	6 hours/day.
Control group and treatment	Air-exposed only.
Duration of test	Females sacrificed on gestation day 18.
Statistical methods	Analysis of variance for body weights, number of resorptions, implants, live, dead or affected fetuses per litter. Significant differences among the groups were also analyzed by Duncan's multiple range test or arcsin transformation of the response proportion. Binary-response variables were between groups were compared using chi-square or Fisher's exact test.
Remarks for Test Conditions.	Female mice were mated to unexposed males and exposed from days 6-15 of gestation to 0, 40, 200, or 1000 ppm of the test substance. Analytical chamber concentrations were measured by on-line gas chromatography. Body weights were recorded on gestation days 0, 6, 11, 16, and 18. Maternal animals were observed daily for mortality, morbidity, and signs of toxicity and examined for gross tissue abnormalities at necropsy (day 18). The uterus and placenta was removed and weighed; the number of implantation sites, resorptions, live and dead fetuses were recorded. Live fetuses were weighed and subjected to external, visceral, and skeletal examinations. Approximately 50% of the fetal heads were sectioned and examined.
Results	
NOAEL maternal toxicity	40 ppm.
NOAEL developmental	40 ppm.
toxicity	There were decreases in maternal body weight gains in the 200 and 1000 ppm groups. Fetal weights were significantly reduced in both males and females at 200 and 1000 ppm; placenta weights were significantly reduced for corresponding male fetuses at 200 ppm and for both males and females at 1000 ppm. There were no significant differences in percent resorptions or malformations per litter, although there was an increase in fetal variations (supernumary ribs and reduced ossification of sternebrae) at 200 and 1000 ppm.
Conclusions	

(study author)	Developmental toxicity was observed in mice in the presence of maternal toxicity at 200 and 1000 ppm. A slight statistically significant decrease in male fetal weight (95% of control) was also observed, but the biological significance of this finding has been questioned.
Data Quality	
Reliabilities	Reliable without restrictions. Guideline study.
References	Morrissey, R.E., Schwetz, B.A., Hackett, P.L., Sikov, M.R., Hardin, B.D., McClanahan, B.J., Decker, J.R., and Mast, T.J. (1990). Overview of Reproductive and Developmental Toxicity Studies of 1,3-Butadiene in Rodents. Environ. Health Perspect. 86:79-84.
Other	Robust Summary Prepared by ExxonMobil Biomedical Sciences, Inc.
La*st changed*	20-Oct-99

Developmental Toxicity/Teratogenicity

Test Substance	
Remarks	1,3-butadiene, CAS# 106-99-0 Purity 99.88%
Method	
Method/guideline followed	OECD 414.
Test type	Developmental toxicity (teratogenicity) study.
GLP	Yes.
Year	1987.
Species	Rat.
Strain	CD (Sprague-Dawley).
Route of administration	Inhalation (gas).
Concentration levels	0, 40, 200, or 1000 ppm.
Sex	24-28 pregnant females per group.
Exposure period	Days 6-15 of gestation.
Frequency of treatment	6 hours/day.
Control group and treatment	Air-exposed only.
Duration of test	Females sacrificed on gestation day 20.
Statistical methods	Analysis of variance for body weights, number of resorptions, implants, live, dead or affected fetuses per litter. Significant differences among the groups were also analyzed by Duncan's multiple range test or arcsin transformation of the response proportion. Binary-response variables between groups were compared using chi-square or Fisher's exact test.
Remarks for Test Conditions.	Female rats were mated to unexposed males and exposed from days 6-15 of gestation to 0, 40, 200, or 1000 ppm of the test substance. Analytical chamber concentrations were measured by on-line gas chromatography. Body weights were recorded on gestation days 0, 6, 11, 16, and 20. Maternal animals were observed daily for mortality, morbidity, and signs of toxicity and examined for gross tissue abnormalities at necropsy (day 20). The uterus and placenta was removed and weighed; the number of implantation sites, resorptions, live and dead fetuses were recorded. Live fetuses were weighed and subjected to external, visceral, and skeletal examinations. Approximately 50% of the fetal heads were sectioned and examined.
Results	
NOAEL maternal toxicity	200 ppm
NOAEL developmental	1000 ppm
toxicity	The only toxicity observed was decreased body weight gains in the dams at 1000 ppm. The percentage of pregnant animals and number of litters with live fetuses were unaffected by treatment. There were no significant differences among the groups for number of live fetuses per litter, percent resorptions or malformations per litter, placental or fetal body weights, or sex ratio.
Conclusions	

(study author)	There was no evidence of teratagenicity or adverse reproductive effects in any of the exposed groups.
Data Quality	
Reliabilities	Reliable without restrictions. Guideline study.
References	Morrissey, R.E., Schwetz, B.A., Hackett, P.L., Sikov, M.R., Hardin, B.D., McClanahan, B.J., Decker, J.R., and Mast, T.J. (1990). Overview of Reproductive and Developmental Toxicity Studies of 1,3-Butadiene in Rodents. Environ. Health Perspect. 86:79-84.
Other	Robust Summary Prepared by ExxonMobil Biomedical Sciences, Inc.
La*st changed*	20-Oct-99

Toxicity to Re production

Test Substance	
Remarks	1,3-butadiene, CAS# 106-99-0 Purity 99.88%
Method	
Method/guideline followed	Other.
Test type	Sperm-head morphology assay.
GLP	Yes.
Year	1987.
Species	Mouse.
Strain	B6C3F1.
Route of administration	Inhalation (gas).
Concentration levels	0, 200, 1000, and 5000 ppm.
Sex	20 males per group.
Exposure period	6 hours/day.
Frequency of treatment	5 days.
Control group and treatment	Air-exposed only.
Duration of test	Males sacrificed 5 weeks post-exposure.
Statistical methods	Normal and abnormal sperm heads were expressed as percentage of the total number of cells examined. These data were subjected to arcsin transformation and evaluated by analysis of variance. If significant, Duncan's multiple range test was used for intergroup differences. Dose response trends were determined by orthogonal contrast.
Remarks for Test Conditions.	The mice were observed twice daily and body weights recorded weekly. During the fifth week post-exposure the mice were sacrificed and examined for lesions of the reproductive tract and other gross abnormalities. Sperm was obtained from the cauda of the right epididymis. Slides were prepared, stained, and examined microscopically. The morphology of at least 500 sperm heads per mouse was categorized.
Results	
NOAEL	200 ppm The percentage of abnormal sperm heads increased with exposure concentration: 1.61% (0 ppm), 1.95% (200 ppm), 2.79% (1000 ppm), and 3.79% (5000 ppm). Only the values for the 1000 and 5000 ppm groups were significantly different from the control ($p < 0.05$). Only a single timepoint was examined, so the effect on all stages of spermatogenesis could not be determined.
Conclusions	
(Study author)	These results suggest that the test substance affected spermatogenesis in mice at 1000 and 5000 ppm, but the effect of this observation on other reproductive endpoints is not known.
Data Quality	
Reliabilities	Reliable with restrictions. Acceptable, well-documented publication which meets basic scientific principles.
References	Morrissey, R.E., Schwetz, B.A., Hackett, P.L., Sikov, M.R.,

	Hardin, B.D., McClanahan, B.J., Decker, J.R., and Mast, T.J. (1990). Overview of Reproductive and Developmental Toxicity Studies of 1,3-Butadiene in Rodents. Environ. Health Perspect. 86:79-84.
Other	Robust Summaries Prepared by ExxonMobil Biomedical Sciences, Inc.
La*st changed*	20-Oct-99

Toxicity to Reproduction

Test Substance	
Remarks	1,3-butadiene, CAS# 106-99-0 Purity 99.88%
Method	
Method/guideline followed	Other.
Test type	Rodent dominant lethal test.
GLP	Yes.
Year	1987.
Species	Mouse
Strain	CD-1 (Swiss).
Route of administration	Inhalation (gas).
Concentration levels	0, 200, 1000, and 5000 ppm.
Sex	20 males per group.
Exposure period Frequency of treatment	6 hours/day. 5 days.
Control group and treatment	Air-exposed only.
Duration of test	8 weeks post-exposure.
Statistical methods	The number of implantation sites and intrauterine deaths per litter for each week were analyzed by analysis of variance. When appropriate, proportions of resorptions and dead or live fetuses per implant were subjected to arcsin transformation and evaluated by analysis of variance. If significant, Duncan's multiple range test was used for intergroup differences.
Remarks for Test Conditions.	After five days of exposure, the male mice were mated with unexposed females (two females per week for each male for 8 consecutive weeks). Females were removed from cohabitation after 7 days sacrificed 12 days later and the uterine contents examined. Observations included: the total number, position, and status of implantations; the numbers of early and late resorptions; and numbers of live and dead fetuses.
Results	Slight statistically significant effects were noted in the mated females for three endpoints during the first 2 weeks post-exposure: ratio of dead to total implants, percentage of females with $\geq$2 dead implants, and number of dead implants per pregnancy. However, these observations only occurred in the two lower exposure groups (except for increased number dead implants/pregnancy in the 5000 ppm group during week 1). There were no differences for number of pregnant females, implantations per litter, number of live fetuses, dead implantations per total implantations, or number of resorptions during weeks 1 and 2. There were no differences for any endpoint during weeks 3-8.
Conclusions	
(Study author)	The authors concluded that the results observed during the first two weeks are consistent with an adverse effect on more mature germ cells (spermatozoa and spermatids) however considering the lack of effects in the high exposure group the findings are not clear for a

	dose-dependent response.
Data Quality	
Reliabilities	Reliable with restrictions. Acceptable, well-documented publication which meets basic scientific principles.
References	Morrissey, R.E., Schwetz, B.A., Hackett, P.L., Sikov, M.R., Hardin, B.D., McClanahan, B.J., Decker, J.R., and Mast, T.J. (1990). Overview of Reproductive and Developmental Toxicity Studies of 1,3-Butadiene in Rodents. Environ. Health Perspect. 86:79-84.
Other	Robust Summary Prepared by Exxon Biomedical Sciences, Inc.
Last *changed*	20-Oct-99

Genetic Toxicity - *in vivo*

Test Substance	
Remarks	C4 Crude Butadiene (Low 1,3-Butadiene Content) approx. composition: 10% 1,3-butadiene, 4% isobutane, 4% n-butane, 29% trans-2-butene, 29% 1-butene, 11% isobutylene, 12% cis-2-butene Primary CAS #: 68476-52-8 Other CAS #s in the stream: 25167-67-3, 64742-83-2, 68187-60-0, 68476-44-8, 68955-28-2, and 68956-54-7.
Method	
Method/guideline followed Type	U.S. EPA OPPTS 870.5395 (1998) and OECD # 474 (1997) guidelines. Mammalian erythrocyte micronucleus assay.
GLP	Yes.
Year	2001.
Species	Mouse.
Strain Sex	B6C3F1 Male and Female
Route of administration	Inhalation (gas).
Doses/concentration levels	0, 0.5, 10.0, or 20.0 mg/L.
Exposure period	4 hours/day for 2 days.
Statistical methods	The raw data on the counts of MN-PCE for each animal were first transformed by adding one (1) to each count and then taking the natural log of the adjusted number. The transformed MN-PCE data and the data on percent PCE were analyzed separately by a two-way analysis of variance (Winer, 1971). The sex-by-dose interaction in the two-way analysis was reviewed and if significant, a one-way analysis was performed for each sex. Pairwise comparisons of treated vs. control groups were done, if the dose effect was significant, by Dunnett's t-test, one-sided (upper) for MNPCE and two-sided for the percent PCE (Winer 1971). Linear dose-related trend tests were performed only if any of the pairwise comparisons yielded significant differences. The alpha level at which all tests were conducted was 0.05.
Remarks for Test Conditions.	Groups of six male B6C3F1 mice (approximately 26g, 9 weeks old) and six female B6C3F1 mice (approximately 21g, 9 weeks old) were exposed whole-body inhalation to target concentrations of 0, 0.5, 10.0, and 20.0 mg/L of the C4 Crude Butadiene, Low 1,3-Butadiene Content. All inhalation exposures occurred under dynamic airflow conditions and chamber concentrations were monitored by analytical methods. Inhalation exposures occurred on two consecutive days, 4 hours per day. A positive control group was dosed by oral gavage with 120 mg/kg of cyclophosphamide approximately 24 hours before sacrifice. Groups of animals (6/sex/dose) were sacrificed at 24 hours after the second treatment for the collection of femoral bone marrow to evaluate the incidence of micronuclei (MN) in polychromatic erythrocytes (2000 PCE/animal) The proportion of PCE among erythrocytes in the bone marrow was estimated by examining 200

	erythrocytes/animal.
Results	Statistically significant increases in the frequencies of MN-PCE in both sexes of all groups treated with the test material were observed as compared to the negative controls. Although statistical analyses indicated a significant dose response, the difference in MN-PCE incidence at the high- (20 mg/L) and low- (0.5 mg/L) dose was minimal. The positive control treatment induced a significant increase in the frequency of MN-PCE. The mean proportion of PCE among the erythrocytes (200/animal) in the bone marrow was not affected following exposure to the test material while the positive control treatment significantly reduced this value.
Conclusions	
(study author)	C4 Crude Butadiene (low 1,3-butadiene content) was positive for the induction of micronuclei in this test system under the experimental conditions used.
Data Quality	
Reliabilities	Reliable without restrictions.
References	Organisation for Economic Co-Operation and Development (OECD) (1997). Guidelines for Testing of Chemicals. #474. Genetic Toxicology: Micronucleus Test, OECD Publication Service, 2 Rue Andre-Pascal, 75775 Paris Cedex 16, France. U.S. EPA (1998). Office of Prevention, Pesticides and Toxic Substances, OPPTS 870.5395. *In Vivo Mammalian Bone Marrow Cytogenetic Tests - Micronucleus assay* Winer, B. J. (1971). *Statistical Principles in Experimental Design* (2nd Edition). McGraw-Hill, New York, New York. Spencer, T.J., Hammond, T.A., Houtman, C.E. and Marty, G.T. (2001). The valuation of C4 crude butadiene (low 1,3-butadiene content) in the mouse bone marrow micronucleus test by an inhalation exposure - multiple exposures followed by a single sampling point. Report of The Dow Chemical Company conducted for the American Chemistry Council, Olefins Panel.
Other	Last updated: Robust summary prepared by contractor to Olefins Panel

Repeated Dose Toxicity

Test Substance	
Remarks	C4 Crude Butadiene (low 1,3-Butadiene Content), approx. composition: 10% 1,3-butadiene, 4% isobutane, 4% n-butane, 29% trans-2-butene, 29% 1-butene, 11% isobutylene, 12% cis-2-butene Primary CAS#: 68476-52-8; Other CAS #s used to represent this stream : 25167-67-3, 64742-83-2, 68187-60-0, 68476-44-8, 68955-28-2, and 68956-54-7
Method	
Method/guideline followed	OECD 422
Test type	Combined repeated exposure inhalation toxicity study with the reproduction / developmental screening test
GLP	Yes
Year	2001
Species	Rat
Strain	Crl:CD® (Sprague-Dawley) IGS BR
Route of administration	Inhalation (vapor).
Duration of test	36-37 days
Doses/concentration levels	0, 2, 10, or 20 mg/L (0; 2,000; 10,000; or 20,000 mg/m^3)
Sex	12 male, 12 female per group.
Exposure period	6 hours/day.
Frequency of treatment	7 days/week
Control group and treatment	12 male, 12 female, air-only exposed.
Post exposure observation period	Not applicable.
Statistical methods	Adult body weights, body weight gains, feed consumption, organ weights, clinical chemistry data and appropriate hematologic data were evaluated by ANOVA. Detailed clinical observation incidence scores for ranked observations and sensory evaluation scores were statistically analyzed by a z-test of proportions. Rectal temperature and grip performance were analyzed by an analysis of covariance with dose as the factor and time as the covariate. Motor activity was analyzed by a repeated-measure design with treatment as a between-subjects factor and the repeated factor of time.
Test Conditions	Groups of 12 male and 12 female CD rats were exposed to vapors of the test material daily by inhalation for approximately six hours/day at exposure levels of 0, 2, 10, or 20 mg/L (0; 2,000; 10,000; or 20,000 mg/m^3). The main study (repeated-exposure general toxicity and neurotoxicity endpoints) males and females were exposed for 36 and 37 days, respectively. Effects on general toxicity, neurobehavioral activity, clinical chemistry, and hematology were evaluated. In addition, a gross necropsy with extensive histopathologic examination of tissues was conducted. The study also contained reproductive and developmental toxicity satellite groups (summarized separately).

Results	
NOAEL (NOEL)	20 mg/L (20,000 mg/mg^3).
LOAEL (LOEL)	Not applicable.
Remarks	Actual time-weighted averages for total olefins for the 2, 10 and 20 mg/L (2,000; 10,000; or 20,000 mg/m^3) exposure groups were **2.17** ± 0.461, **9.81** ± 1.66, **19.1** ± 2.63 mg/L, respectively, over the 37 exposure days in the study. Owing in part to the nature of the test material, there were technical difficulties in generating vapors from the test material, such that targeted exposure concentrations were not met on one entire day and for brief periods on a few other days. However, the affected instances were limited relative to the total duration of the study and were considered to have no significant impact on study integrity. There were no deaths or treatment-related clinical observations noted. No significant differences in body weights or feed consumption were observed for the males or females at any dose level tested throughout the duration of the study. Sensory evaluation, rectal temperature, and fore/hindlimb grip performance data revealed no treatment-related findings. Treatment did not affect motor activity total counts (treatment-by-time interaction, p = 0.0930). However, the treatment-by-time-by-epoch interaction was significant (p = 0.0098). Examination of the data suggested that this effect could be reasonably attributed to the significant time-by-epoch interaction (p = 0.0001) rather than to a true treatment effect. This was confirmed following calculation of linear contrasts to determine which group(s), if any, were different from the control group. These analyses revealed that none of the three treatment groups were significantly different from control (alpha > 0.02) when the time-by-epoch-by-treatment interaction was considered. There were no treatment-related changes for males and females at any dose level for prothrombin time, hematology values or clinical chemistry measures. Females exposed to 2 mg/L had a statistically identified increase in hematocrit value, and a statistically identified decrease in serum total protein. Given the lack of dose response, effects on related parameters, and similar effects in males, these were considered incidental findings that were toxicologically insignificant. There were no effects of exposure on organ weights, gross pathology or histopathology in any of the treated groups when compared to their respective controls.
Conclusions	Repeated inhalation exposure of C4 Crude Butadiene, Low 1,3-Butadiene to male and female Sprague Dawley rats at levels of 0, 2, 10, or 20 mg/L (0; 2,000; 10,000; or 20,000 mg/m^3) produced no evidence of any adverse effects on clinical observations, organ weights, gross or histopathology, neurobehavioral activity, clinical chemistry or hematology endpoints. Based on these data, the no-observable-effect level

	(NOEL) for repeated dose toxicity was 20 mg/L, the highest concentration tested.
Data Quality	
Reliabilities	Klimisch value = 1 (Reliable without restrictions).
References	Carney, E.W., Liberacki, A.B., Thomas, J., Houtman, C.E. and Marable, B.R. (2001). C4 Crude butadiene, low 1,3-butadiene content: a combined repeated exposure inhalation toxicity study with the reproduction/developmental screening test in Sprague Dawley rats. Report of The Dow Chemical Company conducted for the American Chemistry Council, Olefins Panel.
Other	
Last changed	6-Aug-01 Robust summary prepared by contract to Olefins Panel

Toxicity to Reproduction

Test Substance	
Remarks	C4 Crude Butadiene (low 1,3-Butadiene Content) approx. composition: 10% 1,3-butadiene, 4% isobutane, 4% n-butane, 29% trans-2-butene, 29% 1-butene, 11% isobutylene, 12% cis-2-butene Primary CAS#: 68476-52-8; Other CAS #s used to represent this stream: 25167-67-3, 64742-83-2, 68187-60-0, 68476-44-8, 68955-28-2, and 68956-54-7
Method	
Method/guideline followed	OECD 422
Test type	Combined repeated exposure inhalation toxicity study with the reproduction / developmental screening test
GLP	Yes.
Year	2001
Species	Rat
Strain	Crl:CD® (Sprague-Dawley) IGS BR
Route of administration	Inhalation (vapor).
Duration of test	Two weeks prior to breeding, during breeding (up to two weeks), and continuing through day 19 of gestation. The dams were then allowed to deliver their litters, which were retained until postnatal day 4. The males were exposed for 36-37 days.
Doses/concentration levels	0, 2, 10, or 20 mg/L (0; 2,000; 10,000; or 20,000 mg/m^3)
Sex	12 male, 12 female per group.
Exposure period	6 hours/day.
Frequency of treatment	7 days/week
Control group and treatment	12 male, 12 female, air-only exposed.
Post exposure observation period	Not applicable.
Statistical methods	Adult body weights and feed consumption, maternal body weight gains, and pup body weights were analyzed by ANOVA. Gestation length, average time to mating (precoital interval) and litter size were analyzed using a nonparametric ANOVA. Pregnancy rates and mating, conception, fertility and gestation indices were analyzed by the Fisher exact probability test. Evaluation of the neonatal sex ratio was performed by the binomial distribution test. Post-implantation loss, pup survival indices, and other incidence data among neonates were analyzed using the litter as the experimental unit by a censored Wilcoxon test.
Test Conditions	Groups of 12 male and 12 female Sprague Dawley rats were exposed to vapors of the test material daily by inhalation for approximately six hours/day at exposure levels of 0, 2, 10, or 20 mg/L (0; 2,000; 10,000; or 20,000 mg/m^3). The study design included a main study for repeated dose toxicity end points (summarized separately) and reproductive / developmental toxicity satellite groups of 12 females per exposure level. The reproductive and developmental toxicity satellite groups were

	exposed for two weeks prior to breeding, during breeding (up to two weeks), and continuing through day 19 of gestation. Males from the main study were used to breed these females. The dams were allowed to deliver their litters, which were retained until postnatal day 4. Effects on general toxicity, gonadal function, mating behavior, implantation, and general fertility were evaluated in the satellite group adults, followed by a gross necropsy of the satellite group females on lactation day 5. Litter size, pup survival, sex, body weight, and the presence of gross external malformations was assessed in the offspring. The males were exposed for a total of 36 to 37 days, and were then necropsied. In addition to the repeated dose toxicity end points assessed (discussed separately), reproductive assessment of the males included mating, conception and fertility indices, reproductive organ weights and gross/histopathology of the reproductive tract. Testis histopathology included a qualitative assessment of stages of the spermatogenic cycle.
Results	
NOAEL (NOEL)	20 mg/L (20,000 mg/mg^3).
LOAEL (LOEL)	Not applicable.
Remarks	Actual time-weighted averages for total olefins for the 2, 10 and 20 mg/L (2,000; 10,000; or 20,000 mg/m^3) exposure groups were **2.17** $\pm$ 0.461, **9.81** $\pm$ 1.66, **19.1** $\pm$ 2.63 mg/L, respectively, over the 37 exposure days in the study. Owing in part to the nature of the test material, there were technical difficulties in generating vapors from the test material, such that targeted exposure concentrations were not met on one entire day and for brief periods on a few other days. However, the affected instances were limited relative to the total duration of the study and were considered to have no significant impact on study integrity. There were no deaths or treatment-related clinical observations noted. No significant differences in parental body weights, body weight gains or feed consumption were observed at any dose level tested throughout the duration of the study. The only exception to this was a statistically identified increase in feed consumption noted for the 10 mg/L satellite females during the premating period (days 7-14). However, this increase was considered spurious, as feed consumption increases were not noted during subsequent gestation and lactation periods and similar changes in feed consumption were not observed at the highest exposure level of 20 mg/L. There were no treatment-related effects at any dose level on any of the reproductive parameters evaluated in this study. These included measures of reproductive performance (mating, conception and fertility, time to mating, gestation length, litter size), offspring survival (gestation and postnatal survival indices, percent pre- and post-implantation loss), pup body weight and pup sex ratio. The only statistically identified

	change in any of these parameters was an increase in post-implantation loss occurring only at the low-dose. This was considered a spurious finding, given the lack of a dose response. Of the 12 females mated in each group, the number of viable litters produced was 11, 11, 11, and 12 for the 0, 2, 10 and 20 mg/L (0; 2,000; 10,000; or 20,000 mg/m^3) exposure level groups, respectively. External morphological alterations observed in the pups were limited to a hernia observed in a single pup from the high dose group. Given the low incidence of this finding, it was considered spurious and unrelated to exposure.
Conclusions	Repeated inhalation exposure of C4 Crude Butadiene, Low 1,3-Butadiene to male and female Sprague Dawley rats at levels of 0, 2, 10, or 20 mg/L (0; 2,000; 10,000; or 20,000 mg/m^3) produced no evidence of adverse effects on any measures of reproductive function. Based on these data, the no-observable-effect level (NOEL) for reproductive toxicity was 20 mg/L, the highest concentration tested.
Data Quality	
Reliabilities	Klimisch value = 1 (Reliable without restrictions).
References	Carney, E.W., Liberacki, A.B., Thomas, J., Houtman, C.E. and Marable, B.R. (2001). C4 Crude butadiene, low 1,3-butadiene content: a combined repeated exposure inhalation toxicity study with the reproduction/developmental screening test in Sprague Dawley rats. Report of The Dow Chemical Company conducted for the American Chemistry Council, Olefins Panel.
Other	
Last changed	6-Aug-01 Robust summary prepared by contractor to Olefins Panel

Developmental Toxicity/Teratogenicity

Test Substance	
Remarks	C4 Crude Butadiene (low 1,3-Butadiene Content), approx. composition: 10% 1,3-butadiene, 4% isobutane, 4% n-butane, 29% trans-2-butene, 29% 1-butene, 11% isobutylene, 12% cis-2-butene Primary CAS#: 68476-52-8; Other CAS #s used to represent this stream : 25167-67-3, 64742-83-2, 68187-60-0, 68476-44-8, 68955-28-2, and 68956-54-7
Method	
Method/guideline followed	OECD 422
Test type	Combined repeated exposure inhalation toxicity study with the reproduction / developmental screening test
GLP	Yes.
Year	2001
Species	Rat
Strain	Crl:CD® (Sprague-Dawley) IGS BR
Route of administration	Inhalation (vapor).
Duration of test	Two weeks prior to breeding, during breeding (up to two weeks), and continuing through day 19 of gestation. The dams were then allowed to deliver their litters, which were retained until postnatal day 4.
Doses/concentration levels	0, 2, 10, or 20 mg/L
Sex	12 male, 12 female per group.
Exposure period	6 hours/day.
Frequency of treatment	7 days/week
Control group and treatment	12 male, 12 female, air-only exposed.
Post exposure observation period	Not applicable.
Statistical methods	Adult body weights and feed consumption, maternal body weight gains, and pup body weights were analyzed by ANOVA. Gestation length, average time to mating (precoital interval) and litter size were analyzed using a nonparametric ANOVA. Pregnancy rates and mating, conception, fertility and gestation indices were analyzed by the Fisher exact probability test. Evaluation of the neonatal sex ratio was performed by the binomial distribution test. Post-implantation loss, pup survival indices, and other incidence data among neonates were analyzed using the litter as the experimental unit by a censored Wilcoxon test.
Test Conditions	Groups of 12 male and 12 female Sprague Dawley rats were exposed to vapors of the test material daily by inhalation for approximately six hours/day at exposure levels of 0, 2, 10, or 20 mg/L. The study design included a main study for repeated dose toxicity end points (summarized separately) and reproductive / developmental toxicity satellite groups of 12 females per exposure level. The reproductive and developmental toxicity satellite groups were exposed for two weeks prior to breeding,

	during breeding (up to two weeks), and continuing until day 19 of gestation. Males from the main study were used to breed these females. The dams were allowed to deliver their litters, which were retained until postnatal day 4. Effects on general toxicity, gonadal function, mating behavior, implantation, and general fertility were evaluated in the satellite group adults, followed by a gross necropsy of the satellite group females on lactation day 5. Litter size, pup survival, sex, body weight, and the presence of gross external malformations was assessed in the offspring.
Results	
NOAEL (NOEL)	20 mg/L.
LOAEL (LOEL)	Not applicable.
Remarks	Actual time-weighted averages for total olefins for the 2, 10 and 20 mg/L exposure groups were **2.17** ± 0.461, **9.81** ± 1.66, **19.1** ± 2.63 mg/L, respectively, over the 37 exposure days in the study. Owing in part to the nature of the test material, there were technical difficulties in generating vapors from the test material, such that targeted exposure concentrations were not met on one entire day and for brief periods on a few other days. However, the affected instances were limited relative to the total duration of the study and were considered to have no significant impact on study integrity. There were no deaths or treatment-related clinical observations noted. No significant differences in parental body weights, body weight gains or feed consumption were observed at any dose level tested throughout the duration of the study. There were no treatment-related effects at any dose level on any of the reproductive parameters evaluated in this study. These included measures of reproductive performance (mating, conception and fertility , time to mating, gestation length, litter size), offspring survival (gestation and postnatal survival indices, percent pre- and post-implantation loss), pup body weight and pup sex ratio. The only statistically identified change in any of these parameters was an increase in post-implantation loss occurring only at the low-dose. This was considered a spurious finding, given the lack of a dose response. Of the 12 females mated in each group, the number of viable litters produced was 11, 11, 11, and 12 for the 0, 2, 10 and 20 mg/L exposure level groups, respectively. External morphological alterations observed in the pups were limited to a hernia observed in a single pup from the high dose group. Given the low incidence of this finding, it was considered to be a spontaneous finding unrelated to exposure.
Conclusions	Repeated inhalation exposure of C4 Crude Butadiene, Low 1,3-Butadiene to male and female Sprague Dawley rats at levels of 0, 2, 10, or 20 mg/L produced no evidence of developmental toxicity or teratogenicity, as assessed in the OECD 422 study design. Based on these data, the no-observable-effect level (NOEL) for developmental toxicity was 20 mg/L, the highest

	concentration tested.
Data Quality	
Reliabilities	Klimisch value = 1 (Reliable without restrictions).
References	Carney, E.W., Liberacki, A.B., Thomas, J., Houtman, C.E. and Marable, B.R. (2001). C4 Crude butadiene, low 1,3-butadiene content: a combined repeated exposure inhalation toxicity study with the reproduction/developmental screening test in Sprague Dawley rats. Report of The Dow Chemical Company conducted for the American Chemistry Council Olefins Panel.
Other	
Last changed	6-Aug-01 Robust summary prepared by contractor to Olefins Panel

AQUATIC TOXICITY ROBUST SUMMARIES

Fish Acute Toxicity

Test Substance*:	Other TS
Method/Guideline*:	Other: ECOSAR Computer Model
Year (guideline):	1999
Type (test type):	Acute Fish Toxicity Calculation; LC50
GLP:	Not applicable
Year (study performed):	Not applicable
Species: **Analytical Monitoring:**	Freshwater Fish (calculated toxicity values are not species specific) Not applicable
Exposure Period:	96 hours
Statistical Method: (FT - ME)*	Not applicable
Test Conditions: (FT - TC) • **Note: Concentration prep., vessel type, volume, replication, water quality parameters, environmental conditions, organisms supplier, age, size, weight, loading.**	Log Kow (octanol/water partition coefficient) values and a chemical structure are needed to calculate aquatic toxicity using the ECOSAR model. The Kow calculation is performed by KOWWIN based on an atom/fragment contribution method of Meylan and Howard (1), which is a subroutine in the EPIWIN computer model (2). KOWWIN also has a database of experimental Kow values (EXPKOW.DB). The following chemicals are representative of products in the Crude Butadiene C4 Category, which are complex, multi-constituent substances. The range of toxicity data for component chemicals is an estimate of the potential toxicity of category products. Chemical — Calculated log K_{ow} — Measured* log K_{ow} Isobutane — 2.23 — 2.76 n-butane — 2.31 — 2.89 isobutylene — 2.23 — 2.34 cis-butene-2 — 2.09 — 2.31 trans-butene-2 — 2.09 — 2.33 butene-1 — 2.17 — 2.40 1,3-butadiene — 2.03 — 1.99

	* Experimental K_{ow} values supplied by the KOWWIN program database (EXPKOW.DB) which contains more than 13,000 organic compounds with reliably measured values. Commercial products in this category can have a carbon number distribution predominantly between C3 and C5. These products can contain significant levels of 1,3-butadiene and similar low molecular weight olefins, which is why they are considered a category for purposes of the High Production Volume Chemical Program, and designated Crude Butadiene C4. The seven chemicals selected to represent the fish acute toxicity range of this category are C4 hydrocarbons that are common across the 10 CAS numbers (see Test Substance). Crude butadiene category products arise from production processes associated with ethylene manufacturing. More information on the Crude Butadiene C4 Category can be found in the American Chemistry Council, Olefins Panel test plan for this category (3). 1. Meylan, W. and P. Howard. 1995. Atom/fragment contribution method for estimating octanol-water partition coefficients. J. Pharm. Sci. 84:83-92. 2. Meylan, M., SRC 1994-1999. KOWWIN is contained in the computer program EPIWIN. 1999. Estimation Program Interface for Windows, version 3.04. Syracuse Research Corporation, Syracuse, NY, USA. 3. Olefins Panel, HPV Implementation Task Group. 2001. High Production Volume (HPV) Chemical Challenge Program Test Plan For The Crude Butadiene C4 Category. American Chemistry Council, Olefins Panel, HPV Implementation Task Group. VA, USA.
Results: (FT - RS) **Units/Value:** • **Note: Deviations from protocol or guideline, analytical method, biological observations, control survival.**	Calculated fish acute toxicity values for 7 chemicals representative of products in the Crude Butadiene C4 Category are as follows: Chemical — Calculated log K_{ow} — Fish Acute 96-hr LC50 (mg/L) Isobutane — 2.23 — 26.19 n-butane — 2.31 — 22.03 isobutylene — 2.23 — 25.28 cis-butene-2 — 2.09 — 34.23 trans-butene-2 — 2.09 — 34.23 butene-1 — 2.17 — 28.79 1,3-butadiene — 2.03 — 37.59

	Chemical / Measured* log K_{ow} / Fish Acute 96-hr LC50 (mg/L) Isobutane 2.76 8.32 n-butane 2.89 6.28 isobutylene 2.34 19.93 cis-butene-2 2.31 21.26 trans-butene-2 2.33 20.36 butene-1 2.40 17.50 1,3-butadiene 1.99 40.98 * Experimental K_{ow} values supplied by the KOWWIN program database (EXPKOW.DB) which contains more than 13,000 organic compounds with reliably measured values.
Test Substance: (FT - TS)	25167-67-3 Butenes 68477-41-8 Distillate (Petroleum), Extractive C3-5 68955-28-2 Gases, (Petroleum) Light Steam Cracked, Butadiene Concentrate 68476-44-8 Hydrocarbons, >C3 68512-91-4 Hydrocarbons C3 – C4 Rich Petroleum Distillates 68187-60-0 Hydrocarbons, C4, Ethane-Propane Cracked 68476-52-8 Hydrocarbons, C4, Ethylene Manufactured By-Product 68956-54-7 Hydrocarbons C4, Unsaturated 69103-05-5 Hydrocarbons, C4-7, Butadiene Manufactured By-Product 64742-83-2 Naphtha, (Petroleum), Light Steam-Cracked
Conclusion: (FT - CL)	Based on the calculated Kow values, products in this category are expected to have a fish 96-hour LC50 range of 22.03 to 37.59 mg/L. Based on the measured Kow values, products in this category are expected to have a fish 96-hour LC50 range of 6.28 to 40.98 mg/L.
Reliability: (FT - RL)	(2) Reliable with restrictions The toxicity values are calculated.
Reference: (FT - RE)	Cash, G. and V. Nabholz. 1999. ECOSAR Classes for Microsoft Windows, ECOWIN v0.99e. U.S. Environmental Protection Agency, OPPT - Risk Assessment Division. Washington, DC, USA.
Other (source): (FT - SO)	American Chemistry Council, Olefins Panel

* Other TS is an option in the "test substance" pick list within the IUCLID data entry field for " acute toxicity to fish ". Selecting this option refers the reader to information in the "freetext" field for "test substance".

FT - Freetext
IUCLID fields include:
- RL - Reliability
- TC - Test Conditions
- RE - Reference
- RS - Results
- TS - Test Substance
- SO - Source
- CL - Conclusion

Daphnid Acute Toxicity

Test Substance*:	Other TS
Method/Guideline*:	Other: ECOSAR Computer Model
Year (guideline):	1999
Type (test type): **GLP:**	Acute Daphnid Toxicity Calculation; LC50 Not applicable
Year (study performed):	Not applicable
Species:	Daphnid (calculated toxicity values are not species specific)
Analytical Monitoring:	Not applicable
Exposure Period:	48 hours
Statistical Method: (FT - ME)*	Not applicable
Test Conditions: (FT - TC) • **Note: Concentration prep., vessel type, volume, replication, water quality parameters, environmental conditions, organisms supplier, age, size, weight, loading.**	Log Kow (octanol/water partition coefficient) values and a chemical structure are needed to calculate aquatic toxicity using the ECOSAR model. The Kow calculation is performed by KOWWIN based on an atom/fragment contribution method of Meylan and Howard (1), which is a subroutine in the EPIWIN computer model (2). KOWWIN also has a database of experimental Kow values (EXPKOW.DB). The following chemicals are representative of products in the Crude Butadiene C4 Category, which are complex, multi-constituent substances. The range of toxicity data for component chemicals is an estimate of the potential toxicity of category products. Chemical — Calculated log K_{ow} — Measured* log K_{ow} Isobutane 2.23 2.76 n-butane 2.31 2.89 isobutylene 2.23 2.34 cis-butene-2 2.09 2.31 trans-butene-2 2.09 2.33 butene-1 2.17 2.40 1,3-butadiene 2.03 1.99 * Experimental K_{ow} values supplied by the KOWWIN program database (EXPKOW.DB) which contains more than 13,000 organic compounds with reliably measured

values.

Commercial products in this category can have a carbon number distribution predominantly between C3 and C5. These products can contain significant levels of 1,3-butadiene and similar low molecular weight olefins, which is why they are considered a category for purposes of the High Production Volume Chemical Program, and designated Crude Butadiene C4.

The seven chemicals selected to represent the daphnid acute toxicity range of this category are C4 hydrocarbons that are common across the 10 CAS numbers (see Test Substance). Crude butadiene category products arise from production processes associated with ethylene manufacturing. More information on the Crude Butadiene C4 Category can be found in the American Chemistry Council, Olefins Panel test plan for this category (3).

1. Meylan, W. and P. Howard. 1995. Atom/fragment contribution method for estimating octanol-water partition coefficients. J. Pharm. Sci. 84:83-92.
2. Meylan, M., SRC 1994-1999. KOWWIN is contained in the computer program EPIWIN. 1999. Estimation Program Interface for Windows, version 3.04. Syracuse Research Corporation, Syracuse, NY, USA.
3. Olefins Panel, HPV Implementation Task Group. 2001. High Production Volume (HPV) Chemical Challenge Program Test Plan For The Crude Butadiene C4 Category. American Chemistry Council, Olefins Panel, HPV Implementation Task Group. VA, USA.

Results: (FT - RS)

Units/Value:

- **Note: Deviations from protocol or guideline, analytical method, biological observations, control survival.**

Calculated daphnid acute toxicity values for 7 chemicals representative of products in the Crude Butadiene C4 Category are as follows:

Chemical	Calculated log K_{ow}	Daphnid Acute 48-hr LC50 (mg/L)
Isobutane	2.23	28.51
n-butane	2.31	24.11
isobutylene	2.23	27.53
cis-butene-2	2.09	36.91
trans-butene-2	2.09	36.91
butene-1	2.17	31.21
1,3-butadiene	2.03	40.27

Chemical	Measured* log K_{ow}	Daphnid Acute 48-hr LC50 (mg/L)

	Isobutane 2.76 9.39 n-butane 2.89 7.15 isobutylene 2.34 21.86 cis-butene-2 2.31 23.28 trans-butene-2 2.33 22.32 butene-1 2.40 19.28 1,3-butadiene 1.99 43.88 * Experimental K_{ow} values supplied by the KOWWIN program database (EXPKOW.DB) which contains more than 13,000 organic compounds with reliably measured values.
Test Substance: (FT - TS)	25167-67-3 Butenes 68477-41-8 Distillate (Petroleum), Extractive C3-5 68955-28-2 Gases, (Petroleum) Light Steam Cracked, Butadiene Concentrate 68476-44-8 Hydrocarbons, >C3 68512-91-4 Hydrocarbons C3 – C4 Rich Petroleum Distillates 68187-60-0 Hydrocarbons, C4, Ethane-Propane Cracked 68476-52-8 Hydrocarbons, C4, Ethylene Manufactured By-Product 68956-54-7 Hydrocarbons C4, Unsaturated 69103-05-5 Hydrocarbons, C4-7, Butadiene Manufactured By-Product 64742-83-2 Naphtha, (Petroleum), Light Steam-Cracked
Conclusion: (FT - CL)	Based on the calculated Kow values, products in this category are expected to have a daphnid 48-hour LC50 range of 24.11 to 40.27 mg/L. Based on the measured Kow values, products in this category are expected to have a daphnid 48-hour LC50 range of 7.15 to 43.88 mg/L.
Reliability: (FT - RL)	(2) Reliable with restrictions The toxicity values are calculated.
Reference: (FT - RE)	Cash, G. and V. Nabholz. 1999. ECOSAR Classes for Microsoft Windows, ECOWIN v0.99e. U.S. Environmental Protection Agency, OPPT - Risk Assessment Division. Washington, DC, USA.
Other (source): (FT - SO)	American Chemistry Council, Olefins Panel

* Other TS is an option in the "test substance" pick list within the IUCLID data entry field for " acute toxicity to aquatic invertebrates ". Selecting this option refers the reader to information in the "freetext" field for "test substance".

FT - Freetext

IUCLID fields include:

RL - Reliability
TC - Test Conditions
RE - Reference
RS - Results
TS - Test Substance
SO - Source
CL - Conclusion

Alga Toxicity

Test Substance*:	Other TS
Method/Guideline*:	Other: ECOSAR Computer Model
Year (guideline):	1999
Type (test type): **GLP:**	Green Alga Toxicity Calculation; EC50 Not applicable
Year (study performed):	Not applicable
Species:	Freshwater Green Alga (calculated toxicity values are not species specific)
Analytical Monitoring:	Not applicable
Exposure Period:	96 hours
Statistical Method: (FT - ME)*	Not applicable
Test Conditions: (FT - TC) • **Note: Concentration prep., vessel type, volume, replication, water quality parameters, environmental conditions, organisms supplier, age, size, weight, loading.**	Log Kow (octanol/water partition coefficient) values and a chemical structure are needed to calculate aquatic toxicity using the ECOSAR model. The Kow calculation is performed by KOWWIN based on an atom/fragment contribution method of Meylan and Howard (1), which is a subroutine in the EPIWIN computer model (2). KOWWIN also has a database of experimental Kow values (EXPKOW.DB). The following chemicals are representative of products in the Crude Butadiene C4 Category, which are complex, multi-constituent substances. The range of toxicity data for component chemicals is an estimate of the potential toxicity of category products. Chemical — Calculated log K_{ow} — Measured* log K_{ow} Isobutane 2.23 2.76 n-butane 2.31 2.89 isobutylene 2.23 2.34 cis-butene-2 2.09 2.31 trans-butene-2 2.09 2.33 butene-1 2.17 2.40 1,3-butadiene 2.03 1.99 * Experimental K_{ow} values supplied by the KOWWIN program database (EXPKOW.DB) which contains more

	than 13,000 organic compounds with reliably measured values.. Commercial products in this category can have a carbon number distribution predominantly between C3 and C5. These products can contain significant levels of 1,3-butadiene and similar low molecular weight olefins, which is why they are considered a category for purposes of the High Production Volume Chemical Program, and designated Crude Butadiene C4. The seven chemicals selected to represent the alga toxicity range of this category are C4 hydrocarbons that are common across the 10 CAS numbers (see Test Substance). Crude butadiene category products arise from production processes associated with ethylene manufacturing. More information on the Crude Butadiene C4 Category can be found in the American Chemistry Council, Olefins Panel test plan for this category (3). 1. Meylan, W. and P. Howard. 1995. Atom/fragment contribution method for estimating octanol-water partition coefficients. J. Pharm. Sci. 84:83-92. 2. Meylan, M., SRC 1994-1999. KOWWIN is contained in the computer program EPIWIN. 1999. Estimation Program Interface for Windows, version 3.04. Syracuse Research Corporation, Syracuse, NY, USA. 3. Olefins Panel, HPV Implementation Task Group. 2001. High Production Volume (HPV) Chemical Challenge Program Test Plan For The Crude Butadiene C4 Category. American Chemistry Council, Olefins Panel, HPV Implementation Task Group. VA, USA.
Results: (FT - RS) **Units/Value:** • **Note: Deviations from protocol or guideline, analytical method, biological observations, control survival.**	Calculated alga toxicity values for 7 chemicals representative of products in the Crude Butadiene C4 Category are as follows: Chemical — Calculated log K_{ow} — Alga Toxicity 96-hr EC50 (mg/L) Isobutane — 2.23 — 18.06 n-butane — 2.31 — 15.35 isobutylene — 2.23 — 17.44 cis-butene-2 — 2.09 — 23.19 trans-butene-2 — 2.09 — 23.19 butene-1 — 2.17 — 19.71 1,3-butadiene — 2.03 — 25.27 Measured* — Alga Toxicity

	Chemical / log K_{ow} / 96-hr EC50 (mg/L) Isobutane 2.76 6.13 n-butane 2.89 4.71 isobutylene 2.34 13.94 cis-butene-2 2.31 14.81 trans-butene-2 2.33 14.22 butene-1 2.40 12.33 1,3-butadiene 1.99 27.42 * Experimental K_{ow} values supplied by the KOWWIN program database (EXPKOW.DB) which contains more than 13,000 organic compounds with reliably measured values.
Test Substance: (FT - TS)	25167-67-3 Butenes 68477-41-8 Distillate (Petroleum), Extractive C3-5 68955-28-2 Gases, (Petroleum) Light Steam Cracked, Butadiene Concentrate 68476-44-8 Hydrocarbons, >C3 68512-91-4 Hydrocarbons C3 – C4 Rich Petroleum Distillates 68187-60-0 Hydrocarbons, C4, Ethane-Propane Cracked 68476-52-8 Hydrocarbons, C4, Ethylene Manufactured By-Product 68956-54-7 Hydrocarbons C4, Unsaturated 69103-05-5 Hydrocarbons, C4-7, Butadiene Manufactured By-Product 64742-83-2 Naphtha, (Petroleum), Light Steam-Cracked
Conclusion: (FT - CL)	Based on the calculated Kow values, products in this category are expected to have an alga 96-hour EC50 range of 15.35 to 25.27 mg/L. Based on the measured Kow values, products in this category are expected to have an alga 96-hour EC50 range of 4.71 to 27.42 mg/L.
Reliability: (FT - RL)	(2) Reliable with restrictions The toxicity values are calculated
Reference: (FT - RE)	Cash, G. and V. Nabholz. 1999. ECOSAR Classes for Microsoft Windows, ECOWIN v0.99e. U.S. Environmental Protection Agency, OPPT - Risk Assessment Division. Washington, DC, USA.
Other (source): (FT - SO)	American Chemistry Council, Olefins Panel

* Other TS is an option in the "test substance" pick list within the IUCLID data entry field for "acute toxicity to aquatic plants". Selecting this option refers the reader to information in the "freetext" field for "test substance".
FT - Freetext

IUCLID fields include:

- RL - Reliability
- TC - Test Conditions
- RE - Reference
- RS - Results
- TS - Test Substance
- SO - Source
- CL - Conclusion